

# Chapter 1

## Introduction

Cell = the structural & functional unit of <sup>all</sup> living tissues.  
or the smallest unit of living tissues that can exist independently & perform a vital function

### The 4 Basic Tissues :

1. Epithelial tissue
2. Connective tissue
3. Muscular tissue
4. Nervous tissue.

## Microscopes

Magnification power = power of enlargement

Resolution power = the least distance between 2 points that can be seen as 2 points & not one.

Resolution power of naked eye = 0.2 mm.

" " " L.M = 0.2  $\mu$ m

" " " E.M = 0.2 nm.

(N.B) 1 mm = 1000  $\mu$ m

1  $\mu$ m = 1000 nm

1 nm = 10 angstrom ( $\text{\AA}$ )

### 4 Steps to: prepare tissues for Microscopy:

1. Fixation: preserve the tissue:.....
2. Embedding: convert the tissue into solid form to be sliced.
3. Sectioning: into thin section to be examined.
4. Staining: help to identify tissue components & provide visual contrast

### Methods for light microscopy:

- Paraffin technique: most common
- Celloidin technique: most perfect
- Freezing technique: most rapid



VISIT...

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1. Obtain Samples: small pieces [1 cm] are cut [after death, biopsy or experimental animals].

2. Fixation: samples are immediately immersed in fixative:

Fixatives used: formol saline, Bouin, Suzo & Zinker.

Functions of fixatives:

- (1) preserve molecular & morphological structure.
- (2) harden tissues: coagulate their proteins.
- (3) prevent putrefaction: stop autolysis & Kill bact.
- (4) Facilitate cutting & enhance staining

3. Wash in tap H<sub>2</sub>O.

4. Dehydration: H<sub>2</sub>O is removed to be replaced by paraffin [notmissible e' H<sub>2</sub>O] by ascending grades of alc. (to prevent shrinkage of tissues).

5. Clearing in Xylol: [paraffin solvent] to replace alc. (the tissue appears clear).

6. Impregnation: in molten soft paraffin wax (melting point = 50°C) It infiltrates the tissues & replaces Xylol.

7. Embedding: in molten hard paraffin wax (melting point = 55°C) It hardens as it cools, surrounds the tissue → paraffin block hard enough to be cut into thin sections (4-8 μm).

8. Sectioning: by microtome → ribbon of thin sections.

9. Mounting on glass slide smeared e' egg albumin & stained.

| Technique                          | Advantages                                                                                                                                                                                                          | disadvantages                                                                                                                                                             |
|------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <u>Paraffin</u><br>[most common]   | <ol style="list-style-type: none"> <li>1. short time of preparation</li> <li>2. serial sections for research.</li> <li>3. Very thin sections.</li> <li>4. easy staining</li> </ol>                                  | <ul style="list-style-type: none"> <li>- solvents e.g. Xylol dissolve fat</li> <li>- heat damage enzymes → not suitable to show chemical composition of cells.</li> </ul> |
| <u>Celloidin</u><br>[most perfect] | <ol style="list-style-type: none"> <li>1. perfect section for fine details.</li> <li>2. No heat so preserve structure</li> <li>3. suitable for large organs e.g. eye ball &amp; soft tissues e.g. brain.</li> </ol> | <ol style="list-style-type: none"> <li>1. long period.</li> <li>2. No serial sections.</li> <li>3. Thick sections.</li> <li>4. not easily stained.</li> </ol>             |
| <u>Freezing</u><br>[most rapid]    | <ol style="list-style-type: none"> <li>1. most rapid for diagnosis of tumours during surgery</li> <li>2. preserved chemistry, fat &amp; enzymes [histochemistry]</li> </ol>                                         | <ul style="list-style-type: none"> <li>- Difficult cutting →</li> <li>- no serial sections</li> <li>- thick sections</li> <li>- difficult staining.</li> </ul>            |



Scanning E.M.: gives 3 dimensional image

The image will show only the surface of the examined objects.

The most commonly used stain in slides is

Hematoxylin & eosin (H & E)

|                                                                                                         |                             |
|---------------------------------------------------------------------------------------------------------|-----------------------------|
| - Basic stain                                                                                           | acidic stain .              |
| - blue                                                                                                  | - red                       |
| - binds to acidic<br>e.g. nucleus<br>(DNA & RNA)<br>↓<br>cytoplasm of ptn. forming<br>cells (ribosomes) | - binds to basic structures |

Special stains for light microscope.

1. Silver: stains G.A., nerve cells & fibres e' brown colour  
" reticular fibres (brown to black)

2. Neutral stain = Leishman (acidic + basic) for blood cells  
(eosin) methylene  
+ fixative blue  
" methyl alcohol.

3. Vital stain:  
staining living cell inside living animal e.g. stain phagocytic  
cells w' eat the stain e' trypan blue or indian ink.

4. Supravital stain:  
Staining living cell outside living body e.g. staining  
reticulocytes e' Brilliant cresyl blue.

5. metachromatic stain:

the stain will give a new colour diff. from that of the stain  
e.g. When we stain basophils of blood or mast cells of  
c.t. with toluidine blue the content of the granules  
(mucopolysaccharides) react e' the stain giving a violet or  
red colour. This is called Metachromasia.

## Histochemical stains:

stains which show chemical content or enz in the cell

e.g \* Fat stains e' Sudan III → orange  
(frozen section)

\* PAS stains glycogen → magenta red

\* Enzs e.g. acid phosphatase in lysosomes  
[alk. " ]

7. Trichrome stain → 3 stains combined → 3 colors  
for diff. components. Used to demonstrate collagen &c.

8. Orcein: stains elastic fibres (brown)



# The Cell

## Structure

2

It has 2 major components: 1. Cytoplasm 2. Nucleus

### Cytoplasm

#### Organelles

- living structures
- permanent
- Essential
- in all cells
- metabolically active
- have vital function

#### Inclusions

- Non-living
- Temporary
- not essential
- in some cells
- inert
- result from cell activity.

#### Cytosol

- Fluid formed of
- lipids
  - proteins
  - carbohydrates
  - minerals & enzymes
  - Ions & salts
  - $O_2$  &  $CO_2$
  - waste products

### Organelles

#### Membranous

- covered by membrane
- contain enzymes.
- cell memb
- mitochondria
- Endoplasmic Reticulum
- Golgi Apparatus.
- lysosomes.
- peroxisomes.

#### Non-membranous

- Not covered by memb.
- have no enzymes.

##### • Ribosomes

##### • Cytoskeleton :

###### a: Microtubules :

- centrioles
- cilia & flagella.

###### b. Filaments :

- thin filaments.

##### • Proteasomes.



# Cell Membrane

• def.: a living membrane that forms the outer cover of cytoplasm.

• L.M.: cannot be seen as it is very thin (7.5-10 nm)

- can be stained e' Hg or PAS.

• E.M.: 2 dark layers separated by a light one [Trilamellar memb. = Unit memb.]  
The fuzzy layer covering the outer surface = cell coat or Glycocalyx.

## Molecular Structure:

### I. Lipid Component:

#### (a) phospholipids:

molecules arranged in 2 layers [lipid bilayer]. Each molecule has:

1. Hydrophilic polar end = [Head]: (phospholipid)

has affinity to aqueous solutions, so directed outwards (on both sides)  
\* charged.

2. Hydrophobic non-polar end = [Tail]: (Fatty acid)

has no affinity to aqueous solutions, so directed inwards (in the centre)  
\* non-charged.

#### (b) Cholesterol:

small molecules in the hydrophobic zone limiting the movement of molecules  
\* keeping its fluidity.

(N.B) The ratio bet phospholipid : cholesterol = 1:1.

### II. Protein Component: 50% w/w

#### (a) Integral protein:

• embedded in the lipid bilayer

• some extend across the memb. from side to side → [pass/multipass transmembrane proteins].

#### (b) Peripheral protein:

small molecules w form a non-continuous layer loosely attached to both sides of the lipid bilayer.

### III. Carbohydrate component

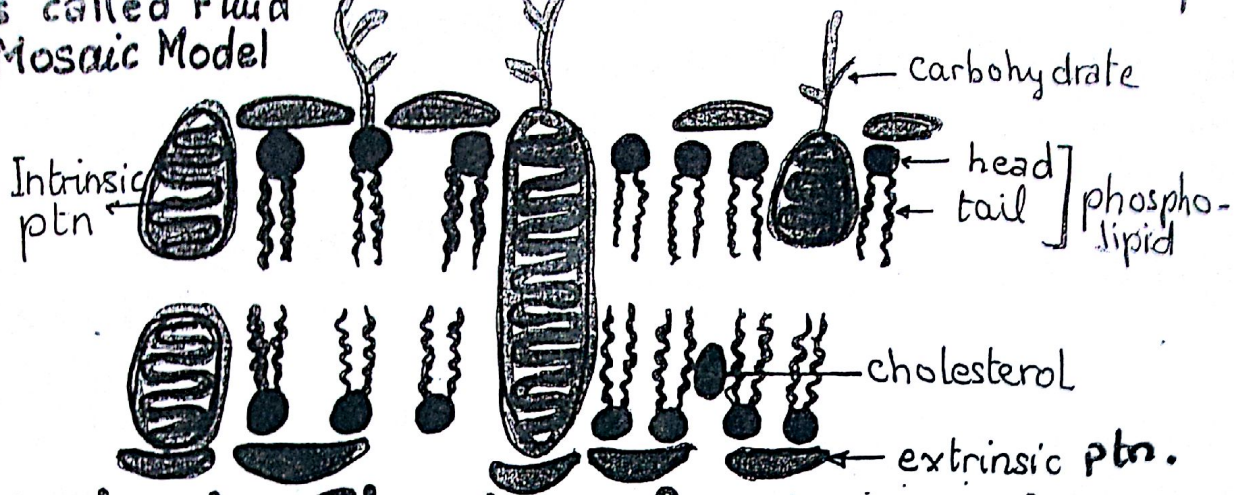
Oligosaccharides linked to ptn. → glycoprotein  
" " lipid → glycolipid } both form cell coat.

### Cell Coat = Glycocalyx:

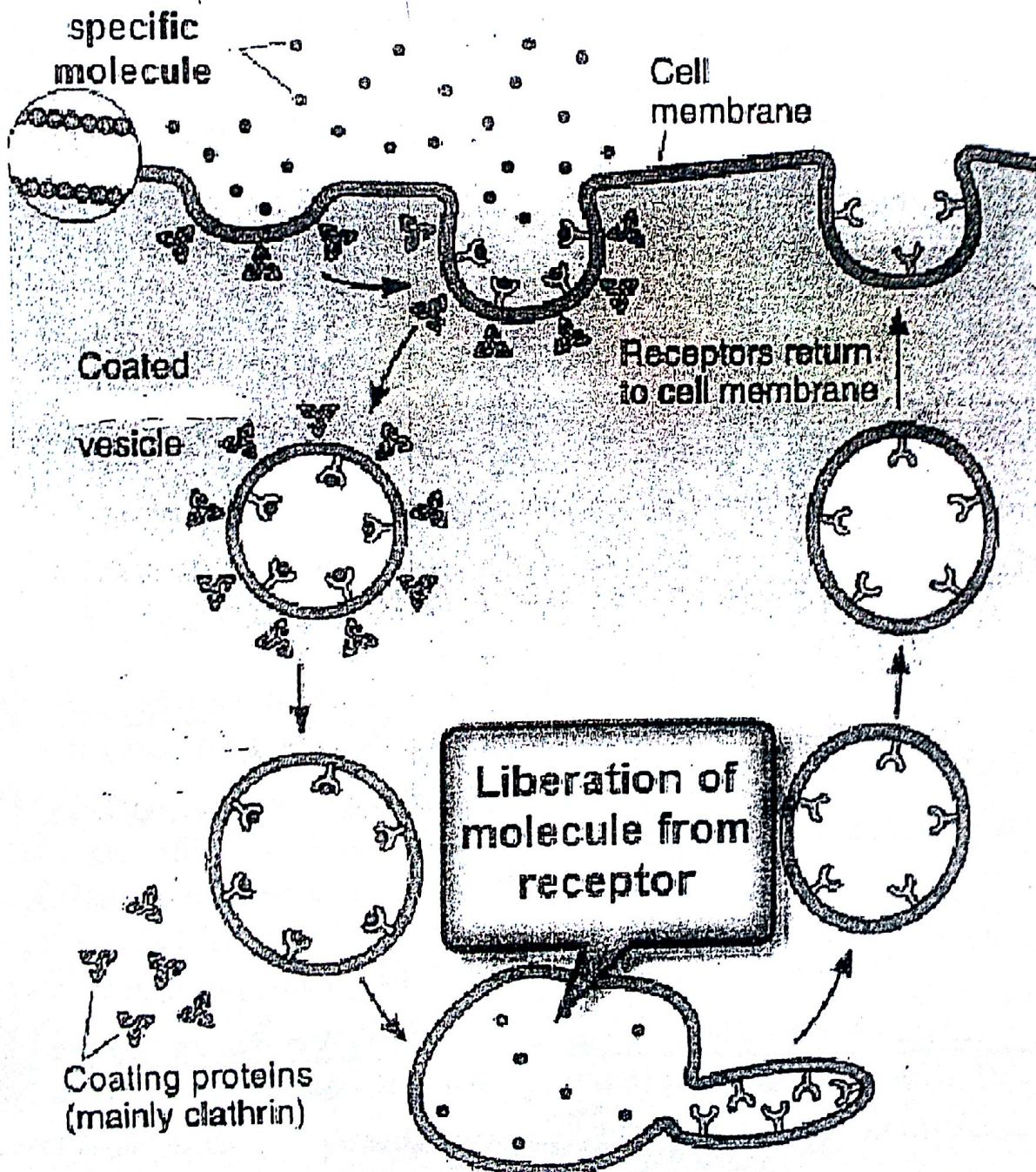
glycoprotein & glycolipid molecules present on the external surface of the cell memb. & rich in receptors that control entrance of bacteria, viruses, drugs & hormones into the cell.



The mosaic appearance of ptns. & Fluid nature of the lipid bilayer is called Fluid Mosaic Model



## Molecular Structure of cell Membrane





## Functions:

### A) Exchange of materials:

- ① Passive diffusion: e.g.  $H_2O$ , ions & gases, controlled by concentration gradient
- ② Facilitated ...: e.g. glucose & a.a.s (do not dissolve in fat) & need transmembrane channels, controlled by conc<sup>n</sup> gradient.
- ③ Active transport: Against conc<sup>n</sup> gradient. needs Energy e.g.  $Na^+/K^+$  pump
- ④ Bulk transport: the cell can take up or release large substances:

#### a. Endocytosis:

##### • Phagocytosis: [Cell eating]:

the cell memb. can engulf bact & damaged cells. When bacteria bind to the surface of macrophage or neutrophil, the cell memb. extends processes that fuse forming a phagosome.

##### • Pinocytosis: [Cell drinking]:

the cell memb. can engulf extracellular fluid. membrane invaginations enclose the fluid forming pinocytic vesicles

##### • Receptor mediated endocytosis:

= integral ptns.

receptors for specific protein hormones & growth factors. Binding of the hormone to the receptors causes the widely dispersed receptors to accumulate in coated pits. their cytoplasmic side are coated w/ Clathrin ptn. The coated pits invaginate & pinch off as coated vesicles carrying the hr. & its receptors.

#### b. Exocytosis:

when a membranous vesicle fuses w/ the cell memb. It releases its contents & the wall of the vesicle is added to the cell memb.

Memb. Trafficking := memb. recycling in Endocytosis & exocytosis.

### B) Cell Coat Functions:

- cell protection
- Cell adhesion
- Cell recognition (identity)
- Cell immunity.

### C) Cell Memb. Modifications:

- Microvilli (↑ surface area for absorption. e.g. absorbing cells of intestine).
- Cilia (move particles in one direction).
- Flagella (form the tail of sperms)
- Stereocilia (non-motile) = long microvilli.

### D) Conduction of excitation waves: in nerve cells & muscles.

**(N.B)** Defective receptors for parathormone & growth hr. in the target organ Causes pseudohypoparathyroidism & dwarfism



# Mitochondria

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Def.: membranous <sup>thread</sup> <sup>granules</sup> organelles responsible for <sup>aerobic</sup> respiration & energy production.  
They are the power house of the cell.

No.: Variable according to cell activity. More numerous in highly active cell  
e.g. few in small lymphocytes & about 1000 in liver cells.

- Can divide by simple division (have their own genetic apparatus DNA).

Site: at site of most activity.

L.M.: appear as rods or granules after staining.

Iron Hx → dark blue or Janus green → green.

E.M.: rounded or oval vesicles 0.5 → 1  $\mu\text{m}$  in diameter & 10  $\mu\text{m}$  in length.

- surrounded by 2 unit membranes separated by intermembranous space

• Outer smooth membrane: contain ptns. called porins, so permeable.

• Inner membrane: less permeable (selective), form shelf like folds (Cristae) projecting into the cavity. to  $\uparrow$  the surface area.

Elementary Particles = globular structures connected to the inner memb. by cylindrical stalks. Globular structures = ptn.  $e^-$  ATP synthetase activity i.e. form ATP in (oxidative phosphorylation)

• Mitochondrial matrix: formed of:

- Oxidative enzs. of Citric A. (Kreb's) Cycle.

- DNA - the 3 types of RNA.

- electron dense granules rich in  $\text{Ca}^{++}$  w act as catalyst for the activity of mitochondrial enzs.

## Functions:

### Cell respiration:

- ① Obtain energy from metabolites in cytoplasm by Kreb's cycle
- ② ~~most~~ of Energy is stored as ATP [by oxidative phosphorylation] & some is dissipated as heat [to maintain body temp].

## Medical application

Mutation in mit. DNA → muscle dysfunction.



# Endoplasmic Reticulum

def.: Communicating membranous channels to form reticulum inside the cytoplasm & enclose a space called Cisterna

2 Types: Rough (granular) ER

Smooth (non-granular)

Sites: excessive in ptn. secreting cells  
e.g. plasma cells & fibroblasts.

Sites in fat & steroid hr. forming cells.  
e.g. liver & endocrine cells.

L.M. basophilia of cytoplasm < <sup>diffuse or</sup> localized

E.M. Parallel cisternae or flattened membranous tubules w̄ extend from nuclear memb. to cell memb. Studded w̄ ribosomes (electron dense) w̄ are bounded to specific receptors [= ribophorins] by their large subunits. Pores under the receptor allow new ptn. to enter & to be stored.

L.M. cannot be seen but when abundant → acidophilia of cytopl.

E.M. branching & anastomosing tubules w̄ smooth surface (no ribosomes).

## Functions:

1. Synthesis of ptn. by the attached polyribosomes.
2. Segregation of the formed ptn.
3. Initial glycozylation of ptn: by addition of monosaccharides.
4. Packing of formed ptn. in transfer vesicles that bud off to be delivered to G.A.
5. Protection of cytoplasm from hydrolytic enzs.
6. Act as intracellular pathway for formed substances.

## Functions:

1. Synthesis of phospholipids of the cell memb.
2. Synthesis of steroid hrs. hormones e.g. cortisol & testosterone
3. Storage & breakdown of Glycogen in liver & muscles
4. Detoxification of drugs & hrs. & alcohol in liver cells.
5. Muscle Contraction by pumping of  $Ca^{++}$
6. Act as intracellular pathway



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def. : membranous organelles responsible for secretion, so well developed in site : secretory cells.

L.M. by (H & E): doesn't appear, but if cytoplasm is deeply basophilic appear as unstained area near the nucleus = -ve Golgi image e.g. plasma cell  
by (Ag): appears as brown granules & fibrils.

by (Ag): appears as brown granules & fibrils.

Sites: • Apical: bet. the nucleus & apex of secretory cells.

- **Perinuclear**: around the nucleus e.g. nerve cells.

E.M.: flattened curved membranous sacculles c' narrow lumen but expanded ends. 3-10 parallel sacculles are arranged one above the other like saucers forming stacks. Each stack has 2 faces:

• Entry (Cis) face:

receives transfer vesicles budding from rER & carry ptn. to G.A.

Exit (Trans) face:

from  $\omega$  diff. vesicles arise. The vesicles may be:

from  $\bar{w}$  diff. vesicles arise. The vesicles may be:

- secretory vesicles: migrate to cell memb. & discharge their contents by exocytosis.
- lysosomes  $\bar{w}$  remain in the cytoplasm & contain hydrolytic enzymes.

Lysosomes remain in the cytoplasm & contain hydrolytic enzymes.

## Functions :

1- Concentration & storage of ptn. formed in rER

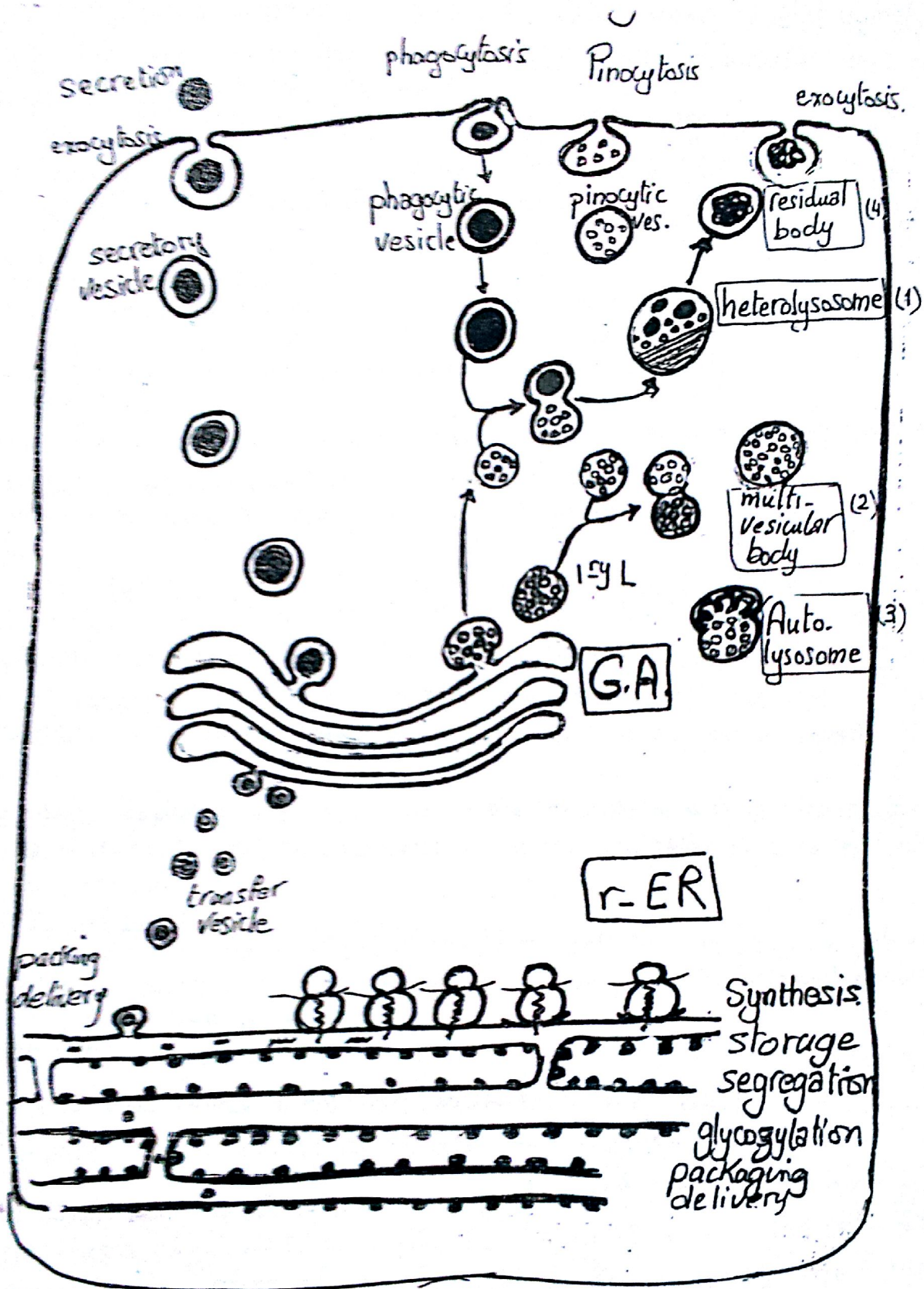
2 Modification of ptn. by addition of  $\begin{cases} \rightarrow \text{carbohydrate} \\ \rightarrow \text{sulfates} \end{cases}$

3. Discharge contents of secretory vesicles  $\left\{ \begin{array}{l} \text{enzymes} \\ \text{hormones} \end{array} \right.$  by **exocytosis**

4- Renewal & Maintenance of cell membrane (integral ptn. is provided from the membranes of secretory vesicles).

5. Formation of lysosomes, & coated vesicles, -







## lysosome

def.: membranous organelles concerned e' intracytoplasmic digestion.

Content: hydrolytic enzymes e.g. lipase, protease, nuclease & acid phosphatase.

Origin: their enzs are ptn. so formed in r.ER, pass as transfer vesicles to G.A. to come out as lysosomes.

Nº abundant in phagocytic cells e.g. macrophages & neutrophil.

L.M. Histochemical tests detect enzs. inside e.g. acid phosphatase.

In macrophages & neutrophils, they are large so can be seen by L.M.

## E.M. 1ry lysosomes

- newly released from G.A. & have not entered digestion.
- membranous vesicle surrounded e' single membrane.
- have homogenous moderately electron dense contents.

## 2ry lysosomes

- When 1ry lysosome fuses e' intracytoplasmic content  $\rightarrow$  2ry lysosome
- appear heterogenous due to the digested material.
- Many types according to type of vesicles 1ry lysosome fuses e' :

### Types:

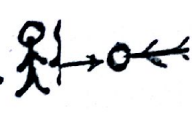
1. Heterolysosome: when 1ry lysosome fuses e' phagocytic vesicle the hydrolytic enzs. digest its contents (food or bact.).
2. Multivesicular body: when 1ry lysosome fuses e' pinocytic vesicle.
3. Autolysosome: when 1ry lysosome fuses e' autophagic vesicle.  
(Vesicle containing old organelles e.g. old mit. i.e. endogenous content).

4. Residual bodies: After digestion of the contents of 2ry lysosomes, the useful material diffuse back to cytoplasm while the undigested retained contents are called residual bodies.

### Fate of residual body:

- either  $\left\{ \begin{array}{l} \text{discharge their contents outside the cell by exocytosis} \rightarrow \text{cytostools.} \\ \text{Or} \rightarrow \text{accumulate as lipofuscin pigment (age pigment) in long lived cells} \\ \text{e.g. nerve cell \& cardiac muscle.} \end{array} \right.$

### Functions:

1. Digest nutrients & foreign invaders e.g. bact.
2. Maintain cell health: eliminate old organelles.
3. Post-mortum autolysis: digestion of the whole cell after death: lysosomes rupture & the enzs digest the cell.  $\rightarrow$  
4. During Fertilization: help the sperm to penetrate the ovum.
5. In thyroid Gland: Activate the hormone

lack of lysosomal sulfatase  $\rightarrow$  intracellular accumulation of sulfated compounds interfering e' the function of nerve cells



## Peroxisomes [Microbodies]

def: membranous organelles similar to lysosomes but contain oxidoreductase enzs. as a.a. oxidase, catalase & peroxidase.

L.M.: cannot be seen.

E.M.: small rounded or oval membranous organelles [0.5  $\mu$ m in diameter]

### Origin:

- the outer vesicle bud off the rER.
- the ptn. of their enzs is formed in free polysomes.
- the enzs. are recognized & internalized by receptors on their memb.

### Functions:

- Oxidation of long chain Fatty acids forming  $\xrightarrow{\text{Acetyl CoA}} \text{Acetyl CoA [CoA]}$   
 $\xrightarrow{\text{H}_2\text{O}_2}$
- Acetyl CoA is used by the cell
- $\text{H}_2\text{O}_2$  kills microorganisms & detoxifies agents as ethanol.
- Excess  $\text{H}_2\text{O}_2$  (toxic) is reduced by catalase to  $\text{H}_2\text{O} + \text{O}_2$

N.B.

Energy produced is not stored as ATP but comes out as heat.

### Medical application

#### Fatal medical Syndrome:

deficiency of peroxisomal enzs.  $\xrightarrow{\quad}$  muscular dystrophy.  
 E.M. shows empty peroxisomes  $\xrightarrow{\quad}$  liver & kidney lesions.



# Non-Membranous Organelles

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## 1- Ribosomes

def.: Non-membranous electron dense bodies, (20x30 nm)

Formed in: nucleolus & pass to cytoplasm through nuclear pores.

Origin: Formed of: r-RNA (formed in nucleolus) + ptn. (formed in cytoplasm)

No.: Abundant in ptn. forming cells.

L.M. too small, so cannot be seen but when abundant  $\rightarrow$  basophilia of cytoplasm  
 $\bar{w}$  may be \* Diffuse: e.g. in embryonic cells.

\* Localized: e.g. at the base of the cell as in pancreas.

\* Spotty: e.g. Nissl granules in nerve cells.

E.M. Small dense granules. Formed of 2 subunits (small & large)  $\bar{w}$  attach by m-RNA. The large subunit contains a groove in its centre  $\bar{w}$  contains the polypeptide chain. There are 2 forms:

### 1- Free ribosomes:

scattered singly or as Polysomes [Polyribosomes]:

linked by m-RNA  $\rightarrow$  rosette-shaped or spiral aggregations.

2- Attached: to rER by its large subunit at glycoprotein receptors = ribophorins. They are attached to m-RNA that carry the information of sequence of a.a.s.  
t-RNA picks up a.a.s & transports them to the ribosomes  
 $\bar{w}$  reads & translates the code & form the polypeptide chain  
 $\bar{w}$  is injected into the lumen of rER cisternae.

Function: ptn. synthesis.

### 1- Free ribosomes:

form ptn. used inside the cell e.g. glycolytic enzs.  
(build)

### 2- Attached ribosomes:

form ptn. secreted by the cell e.g. enz. or hormones.



## [2] Cytoskeleton

Microtubules + filaments + some ptns.  $\rightarrow$  bind them to each other & to cell memb.  $\rightarrow$  Microtrabecular lattice.

### A] Microtubules

def.: fine tubes of constant diameter (24 nm) but unfixed length.

L.M.: cannot be seen except by using immunofluorescent technique.

E.M.: fine tubules formed of  $\alpha$  &  $\beta$  ptn. called tubulin that arrange in

13 protofilament. Their length change by polymerization of tubulin. This is directed by Microtubular Organizing Centre  $\rightarrow$  contain gamma tubulin.

### 2 Forms:

#### • Dynamic form:

e' continuous assembly & disassembly  $\rightarrow$  cell reshaping

• Stable form: in wall of centrioles, cilia & flagella

#### functions:

1. Cytoskeleton  $\rightarrow$  preserve cell shape
2. Form mitotic spindle during cell division.
3. Intracellular transport of molecules
4. Form centrioles, cilia & flagella.

Chemotherapy arrest cell proliferation in Cancer (tumours) by interfering e' M.T. assembly.

### B] Filaments

def. minute ptn. threads. 2 forms:

1. Thin = Actin = microfilaments: 6 nm  
Fine strands of 2 chains of globular G actin coiled to form filamentous F actin

#### Sites & functions:

##### ① In most cells:

- a. Form a network under the cell memb.  $\rightarrow$  cell shape changes e.g. endo or exocytosis & amoeboid movements.
- b. movement of organelles or vesicles. (cytoplasmic streaming)
- ② In dividing cells:  $\rightarrow$  cleavage of mitotic cells.
- ③ In skeletal ms: together e' thick myosin  $\rightarrow$  muscle contract.
- ④ In Microvilli: form their core, give their shape, their shortening & elongation helps absorption.

##### ② Intermediate filaments: 10 nm

A family of filaments formed by polymerization of tetrameric subunits  $\rightarrow$  differ chemically 6 types:

1. Keratin: in epithelium, hairs & nails.
2. Vimentin: in muscle & c.t.
3. Desmin: in muscles to join myofibrils.
4. Neurofilaments: in neurones
5. Glial fibrillary acidic ptn: in glial cells.
6. lamins: in nuclear envelope.

Immunocytochemical methods are important for Diagnosis & treatment of tumors by diagnosis the cell of origin by the type of filaments in that tumor.



## Structures formed by Stable Microtubules

### 1. Centrioles

**def:** non-membranous organelle in an area of cytoplasm near the nucleus = Centrosome

**L.M.:** appear as 2 small dark bodies in the centrosome after staining e' iron Hx

**E.M.:** 2 hollow cylinders perpendicular to each other.

- In cross section, its wall is formed of 9 bundles of microtubules, each bundle is formed of 3 microtubules (triplets) i.e.  $9 \times 3 = 27$  microtubules.

- The inner microtubule (A) is complete while B & C microtubules share the wall of the adjacent one.



A = 13 protofilament  
B & C = 10 " "

**Functions:** [interphase]

1. **Cell division** | the 2 centrioles duplicate  $\rightarrow$  2 pairs, each pair migrates to one side of the cell & become surrounded by area of cytoplasm rich in tubulin called **MTOC**. From w microtubules arise  $\Rightarrow$  **mitotic spindle**.

2. **Form Cilia & Flagella.**

### 2. Cilia

**def:** motile hair like processes formed of a core of microtubules covered by cell memb.

**Origin:** during development, centrioles duplicate many times & give basal bodies w migrate to the apex to give cilia.

**L.M.:** acidophilic striations (hair like)

**E.M.:** Each cilium is formed of 3 parts:

1. **Basal body:**

= a centriole i.e. 27 microtubules in 9 triplets embedded in the cytoplasm.

2. **Shaft = axoneme.**

- Finger like projection covered e' cell memb.

- From each triplet, the inner 2 MTs. A & B linked by nexin  $\rightarrow$  doublets.

i.e. the shaft = 9 bundles of doublets + 2 single microtubules in the centre (singlets). So the shaft is formed of  $[(9 \times 2) + 2] = 20$  microtubules.

3. **Rootlets:**

- Formed by growth of the 3<sup>rd</sup> (outer) microtubule (c) in each triplet into the cytoplasm i.e. 9 microtubules. It fixes the basal body & shaft to cytoplasm.

**Functions:**

1. Their rhythmic beating move fluids or particles in one direction by axonemal dynein

e.g. respiratory system & ♀ genital system.

2. Modified cilia act as receptors e.g. rods & cones of retina.

### 3. Flagella

Single extra long shaft of cilium =  $[9 \times 2 + 2] = 9$  peripheral doublets + 2 central singlets e.g. form the tail of sperm. Its whip like movement helps to move the sperm.



Immotile Cilia Syndrome:

Immotile sperms  $\rightarrow$   $\sigma$  infertility + chronic respiratory infections

### 3 Proteasomes

def. : Non-membranous organelle that degrades ptn. molecules attached to ubiquitin ptn. through ATP-dependent pathway.

E.M.:

A barrel-shaped core particle = 4 rings stacked over each other. At both ends of the " " is regulatory particle that contain ATPase & recognize ptns attached to ubiquitin molecules.

Functions:

1. remove excess enzs & unnecessary ptns.
2. " ptns. that are incorrectly folded.
3. destroy " infected by viruses.

Defective proteasomes lead to accumulation of unwanted ptns related to Alzheimer's disease.



## Cell Inclusions

def. : Non-living, temporary structures, not present in all cells inert, result from cell activity. Include :

A-stored food    B. pigments    C. crystals.

### A. Stored Food

#### [1] Carbohydrates :

stored as glycogen in  $\left\{ \begin{array}{l} \text{liver \& } \\ \text{muscle cells.} \end{array} \right.$

- L.M. : By H & E appear as vacuoles.

e' Best's carmine  $\rightarrow$  red    e' PAS  $\rightarrow$  magenta red

- E.M.

2 types : a - granules : single granules

B. granules : rosette-shaped aggregates

- Site : at areas rich in s.ER.

#### [2] Fats :

stored as fat droplets e.g. in liver cells or  
" globules " " fat cells.

- L.M. By H & E appear as vacuoles

By Sudan III  $\rightarrow$  orange.

### B. Pigments

def. : materials that possess color of their own

types : 1. Exogenous :

taken from outside

e.g a. Carbon & dust as in dust cell of lung

b. Carotene : taken e' food  
e.g. carrots.

c. Tattoo marks : injected  
under the skin & taken  
by phagocytic cells.

2. Endogenous :

formed by the cell

a. Hb in RBCs to carry  $\left\{ \begin{array}{l} O_2 \& \\ CO_2 \end{array} \right.$

b. melanin in skin & eye :  
give its color & protect from  
ultra violet rays (UVR.)

c. lipofuscin : in long lived cells  
e.g. nerve cell & cardiac muscle  
they are waste products of age.



## Nucleus

- def. The largest component of the cell. present in all cells except: RBCs & platelets (not true cells)
- No. : usually one, some cells are binucleated (2 nuclei) e.g. liver cells & some are multinucleated (many nuclei) e.g. osteoclasts & skeletal muscles
- Position : usually central, may be eccentric, basal or peripheral.
- Shape : rounded, oval, flat, kidney-shaped, bilobed (horse-shoe), segmented or lobulated.
- L.M. : basophilic due to RNA & DNA. (Hx or methylene blue)
- Appearance : either:
  - \* Lightly stained (Vesicular) : pale (open face) e' extended chromatin & prominent nucleolus e.g. nerve cells.
  - \* Deeply stained (Condensed) : dark (closed face) e' condensed chromatin e.g. small lymphocyte

## Structure of Nucleus

### I] Nuclear membrane [envelope]

- L.M. basophilic line (due to ribosomes outside & chromatin inside)
- E.M. 2 membranes separated by perinuclear space & interrupted by nuclear pores (30-50 nm)
- 1. Out. rough membrane: due to attached ribosomes & continuous e' r.E.R.
- 2. Inner fibrillar " : e' "associated" chromatin threads on its inner surface

### Nuclear Pore Complex:

Formed of transmembrane ptns. w form an octagonal annulus (ring)  
Nucleoporin filaments extend into the cytoplasm & nucleus

### Function:

- a. transport of proteins to the nucleus
- b. export of RNA & ribosomes to the cytoplasm ] through receptor proteins

### II] Chromatin Material:

def. basophilic particles or threads that change into chromosomes during division  
chemically: DNA + ptn (histone)

#### Types a) Euchromatin [extended or active]:

(L.M.) extended parts of chromatin so pale by L.M. (vesicular)  
carry active genes w direct ptn. synthesis in ptn. forming cells:

#### b) Heterochromatin [condensed or inactive]:

- coiled parts of chromatin so dark by L.M. (condensed)
- carry inactive genes.



E.M.: 1. Euchromatin = fine granules.

2. Hetero " " = Condensed masses at 3 sites:

a. peripheral chromatin: attached to inner nuclear memb.

b. chromatin islands: clumps scattered in the sap.

c. nucleolus associated chromatin: around nucleolus.

### Functions of chromatin:

1. Carry genetic information.

2. Direct ptn. synthesis.

3. Form 3 types of RNA  $\leftarrow$  r.RNA.

V.B. Chromosomal alterations  $\leftarrow$  E.RNA: Tumours or genetic diseases.

### III Nucleolus:

L.M. one or 2 basophilic rounded masses rich in nucleic acids.

E.M. Spongy appearance = dark & light areas: not limited by membrane.

dark areas = pars amorpha = central filaments of DNA [nucleolar organizer]

pars fibrosa = strands of newly formed r.RNA

pars granulosa = granules of mature r.RNA (ribosomes)

both pars fibrosa & granulosa are called nucleolonema.

Light areas = nucleolar sap.

Functions: Formation of r.RNA & ribosomes w pass through nuclear pores to cytoplasm to form protein. So, ptn-forming cells have prominent nucleoli (1 or 2)

### IV Nuclear Sap:

def: solution that fills the spaces bet. chromatin & nucleolus. Formed of: nucleoptns, sugars, enzymes, Ca, K & phosphorus ions.

Funct? act as medium for transport of RNA to nuclear pores  $\rightarrow$  cytoplasm.

Rapidly growing malignant cells have large nucleoli.

### Functions of the Nucleus

1. Controls all functions & ptn. synthesis.

2. Form all types of RNA.

3. directs cell division.

4. Carry genetic information & heredity factors.



# Cell Cycle

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A series of changes to prepare the cell for division. 2 phases:

1. Mitosis: [1 hr.] Changes are visible e' L.M.
2. Interphase [20 hrs] " " " not seen " = period bet. 2 successive divisions.  
the cell grows, does specific function & replicates its genetic material.

## a) Gap 1 (G<sub>1</sub>) phase: [8 hrs]

- the nucleus contains 46 chromatids (Single S-chromosomes)
- the daughter cells grow in size, acquire energy & start ptn. synthesis for duplication of DNA. The cell become specialized.
- the more specialized the more prolonged G<sub>1</sub> & less rate of division.

## b) Synthesis (S) phase: [8 hrs].

- duplication of DNA → double (d-chromosomes)
- " " " centrioles.

## c) Gap 2 (G<sub>2</sub>) phase: [4 hrs].

- any error in DNA replication is corrected.
- second growth (synthesis of RNA) & storage of energy for next mitosis.
- synthesis of tubulin to build microtubules needed for mitosis.

• G<sub>0</sub> (Outside or Stable) phase := cells that have left the cycle (resting stage)

## • Cell Cycle Check points:

G<sub>1</sub>, G<sub>2</sub> & M check points to ensure that the processes at each phase of the cycle have been completed before progressing to the next phase.

# Cell Renewal

Most of specialized cells are in prolonged G<sub>1</sub> of interphase.

There are 3 types of specialized cells according to their ability to reproduce.

## 1] Non-Renewing Cells:

Highly specialized cells leave the cycle in G<sub>1</sub> to G<sub>0</sub> = (permanent exit)

Never divides again & cannot be replaced by new ones. e.g. Cardiac cell + nerve cell

## 2] Potentially Renewable Cells:

Specialized cells w leave the cycle in G<sub>1</sub> to G<sub>0</sub> but returns back on need

for renewal (transient exit) e.g. liver cells when destroyed or partially removed can restore their normal size.

## 3] Continuously renewing Cells:

Specialized cells w cannot divide, but replaced from stem cells e.g.

blood cells & Sperms.



## Stem Cells

2 types:

• Pluripotential [multipotential] Stem cells:

Have the potential to give > one type of specialized cells e.g. blood cells & cells lining gastro-intestinal tract [GIT].

• Unipotential stem cells: able to produce only one type of specialized cells e.g. germ cells

## Cell Death

### Necrosis

pathological condition

results from  $\begin{cases} \text{anoxia} \\ \text{toxins} \\ \text{mechanical injury} \end{cases}$

The cell & its organelles swell then burst & release their contents in the extra cellular space & finally phagocytosed by macrophages.

### Apoptosis

- programmed cell death.

- occurs normally at end of life span.

- cells do not swell but ↓↓ in size

- Nuclei show:

\* pyknosis: become small, dark & condensed chromatin

\* Karyorrhexis: " fragmented into pieces by endonuclease enz

\* Karyolysis: dissolution then disappear.

- Cytoplasm breaks → vesicles phagocytosed by macrophages.



## Mitosis

Def.: the process by which the cell divides into 2 equal cells genetically identical to the parent cell. 4 Stages:

### 1. Prophase:

- The 46 chromosomes become, shorter, thicker, darker & appear as threads
- The nuclear membrane & nucleolus disappear.
- Each pair of centrioles move towards one pole of the cell by growth of microtubules from the microtubular organizing centre (MTOC) around the centrioles. Microtubules form the mitotic spindle.

### 2. Metaphase:

- Chromosomes migrate to the equatorial plane [Metaphase plane].
- At the centromere, each chromosome develops a disc like Kinetochore to which chromosomal microtubules attach
- ∴ the mitotic spindle is formed of:
  - Cytoplasmic microtubules: arise from MTOC around centrioles to elongate the cell. (continuous)
  - Chromosomal " ": arise from MTOC attached to Kinetochores [non-continuous]
    - ↳ arrange chromosomes in equatorial plane
    - ↳ pull sister chromatids apart.
  - Astral microtubules: arise from MTOC around centrioles in a star like fashion to establish the axis of the spindle.

### 3. Anaphase:

- Chromosomes split longitudinally at the centromere into 2 chromatids which migrate towards the opposite poles by interaction between chromosomal & cytoplasmic microtubules.

### 4. Telophase:

- A constriction develops at the equatorial plane [cleavage furrow] by contraction of actin microfilament. It deepens until the cell divides into 2.
- The 46 chromatids (s-chromosomes), start to uncoil, lengthen & become invisible
- The nuclear memb. & nucleoli reappear.



# Meiosis

It is a type of division in which the diploid mother cells in the testis & ovary undergo 2 successive divisions without S-phase to produce haploid germ cells (sperms or ova).

## First Meiotic division [Reduction division]

### 1. Prophase (I):

22 days in ♂ & 12-45 years in ♀. 5 stages:

#### a. Leptotene: [thin ribbon]

The 46-d. chromosomes appear as long thin separate threads.

#### b. Zygotene:

The chromosomes are arranged in 23 pairs = **bivalents**. Each pair is formed of 2 homologous chromosomes: [1 maternal & 1 paternal] alongside each other.

#### c. Pachytene: (thick)

- Chromosomes become shorter & thicker & appear as tetrads of 4 chromatids.
- segments of the chromatids may break by recombinase enzyme.
- The segments rejoin & exchange of segments bet. the non-sister chromatids of homologous chromosomes. [**Crossing Over**]
- The region of crossing over is called **Chiasmata**.

#### d. Diplotene: (double)

- Chromosomes continue to condense & separate revealing chiasmata.

#### e. <sup>across move</sup> Diakinesis:

- Chromosomes condense maximally.
- nucleolus & nuclear membrane disappear. freeing chromosomes in the cytoplasm.

### 2. Metaphase (I)

Mitotic spindle is well developed & the 23 bivalent chromosomes are arranged in the equatorial plane & attached to the microtubules of the spindle.

### 3. Anaphase (I):

- Each chromosome of a bivalent moves to one pole of the cell.

### 4. Telophase (I):

The 2 daughter cells are formed each with 23 d. chromosomes.



## Second Meiotic Division [equatorial division]

Mitosis like e' very short interphase (e' out s-stage). Each daughter cell has 23 d-chromosomes.

### 1. Prophase (II):

- Chromosomes become shorter & thicker.
- Mitotic spindle starts to appear.

### 2. Metaphase (II):

- the 23 d-chromosomes are aligned at the equatorial plane.

### 3. Anaphase (II):

- Each d-chromosome splits at the centromere  $\Rightarrow$  2 chromatids each moves to one pole of the cell. (s-chromosomes)

### 4. Telophase (II):

- The 2 daughter cells separate, each e' 23 s-chromosome.

| Mitosis                                                                                                                                                                                                                                                                                                                                                                                                                | Meiosis                                                                                                                                                                                                                                                                                                                                                                                                                         |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>- In somatic cells.</li> <li>- Single division <math>\rightarrow</math> 2 daughter cells e' diploid No. of chromosomes.</li> <li>- daughter cells are genetically identical.</li> <li>- No pairing <math>\rightarrow</math> No crossing over</li> <li>- no exchange of genes.</li> <li>- Each chromosome divides longitudinally at the centromere into 2 chromatids.</li> </ul> | <ul style="list-style-type: none"> <li>- In germ cells of &lt; testis &amp; ovary.</li> <li>- 2 successive divisions <math>\rightarrow</math> (e' out s-phase) 4 daughter cells e' haploid No. of chromosomes (show genetic variation)</li> <li>- pairing allows crossing over</li> <li>- exchange of genes.</li> <li>- Each chromosome of a bivalent migrates to one pole of the cell (in 1<sup>st</sup> division).</li> </ul> |



# Human Chromosomes

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= Chromatin fibres  $\bar{w}$  become so coiled & condensed so, become visible e' L.M  
At  $G_1$  of interphase: the chromosome is a single thread = s. chromosome  
At S. stage: " " " is double threads = d. " "

At Metaphase & late prophase:

- \* each chromosome is formed of 2 chromatids joined at the centromere  $\bar{w}$  divides the chromosome into 2 arms: short arm (p) & long arm (q).
- Kinetochore = 2 discs of ptn. at both sides of the centromere to  $\bar{w}$  spindle fibres are attached.
- Each chromatid = DNA molecule coiled around histone & non-histone ptns
- genes = segments of DNA that code for specific ptn. Each gene has a specific position (locus)
- Telomere: the terminal end of the chromosome. Has a repeated sequence of bases to protect the end of the chromosome & prevent end to end fusion of chromosomes.

## \* Classification of Chromosomes:

### A) According to length:

- 22 homologous pairs are numbered serially from 1-22, then grouped into 7 groups in a descending order of length: (A, B, C, D, E, F & G)
- the sex chromosomes are either arranged alone or X in group C & Y in group G.

### B) According to position of centromere:

1. Metacentric: centromere at the centre i.e. the 2 arms are equal  $p=q$ .
2. Submetacentric: " " midway bet. the centre & the upper end i.e.  $p < q$ .
3. Acrocentric: " " close to one end ( $p$  is very short). Some of them have small mass of chromatin = Satellite attached to  $p$  arm by 25y constriction containing genes for r-RNA. (except in Y. chromosomes).
4. Telocentric: centromere is terminal i.e. no short arm. Not in humans.

### C) According to genes:

1. Autosomes: 22 homologous pairs = control somatic characters
2. Sex chromosomes: 1 pair = control sex
  - homologous (identical) XX in ♀
  - heterologous (unidentical) XY in ♂



## Karyotyping

def. : the study of the No & types of chromosomes according to their length & position of the centromere.

Technique : WBCs are the best cells to study chromosomes.

1. A heparinized blood sample is obtained (prevent clotting)
2. the sample is centrifuged to separate WBCs.
3. WBCs are incubated in a culture medium to w a mitogenic factor is added. at  $37^{\circ}\text{C}$  for 3 days. (phytohemagglutinin)
4. Colchicine is added to stop cell division at metaphase.
5. Hypotonic solution is added so cells swell & chromosomes disperse
6. Cells are spread on a slide, fixed, stained e' Giemsa & photographed.
7. Chromosomes in the photo are cut, matched into pairs & arranged according to their length & position of centromere.

## Banding Technique:

It can differentiate chromosomes by staining different segments [genes] by different colours.

## Clinical Importance of chromosomal Examination

1. Identification of sex  $\begin{cases} \rightarrow \text{in Foetus (in cells in amniotic fluid)} \\ \rightarrow \text{" doubtful cases of hermaphroditism.} \end{cases}$
2. Diagnosis of abnormalities in sex chromosomes e.g. Turner's syndrome (XO) & Klinefelter's syndrome (XXY).
3. Diagnosis of numerical abnormalities in chromosomes e.g. Mongolism.
4. Diagnosis of structural " " " " " " e.g. deletion in mental retardation & translocation in chronic myeloid leukemia.
5. Medico legal importance in Forensic Medicine.



## **Sex Chromatin [Barr body]**

- Dark mass of chromatin, present in :
  - 60% of ♀ epithelial cells lining the buccal cavity: appear a dark body inner to the nuclear membrane.
  - 3-5% of ♀ neutrophils: appear as drum stick-like mass attached to the nucleus.
  - It represents inactive coiled X-chromosome. The other X is active, extended & not apparent.
  - It appears in ♀ cells & in ♀ e' Klinefelter syndrome [XXY]
  - Absent in ♂ cells & in ♀ e' Turner syndrome [XO].
- (N.B) Somatic cells have at least 1 X-chromosome w must be active, extended & not visible). It carries other genes (not sex determining).

## **Chromosomal Aberrations**

def.: deviation from the normal N<sup>o</sup> or structure of chromosomes.

- Most of abnormalities cause - mental retardation
- developmental " "

### **Causes of chromosomal aberrations :**

1. Viral Infection: e.g. german measles → Fragmentation of chromosomes
2. Radiation: → chromosomal damage & non-disjunction.
3. Drugs e.g. cytotoxic drugs e.g. colchicine → inhibit mitotic spindle
4. Pregnancy in old women ⇒ ↑↑ risk of non-disjunction (long prophase)
5. Auto. immune disease: associated e' non-disjunction.



# I-Numerical Aberrations

**a) Euploidy:** - multiple of haploid  $N^o$  & exceeds the diploid  $N^o$ .

1. Triploidy =  $3n = 69$  chromosome.

2. Tetraploidy =  $4n = 92$  "

due to failure of 1st cleavage of the fertilized ovum.

3. Polyploidy  $\geq 5n$ : one or both gametes are not haploid.

**b) Aneuploidy:**

abnormal  $N^o$  is not the exact multiple of the haploid  $N^o$ .  
e' addition or loss of a chromosome. Types:

1. **Trisomy:**  $2n+1$  e' addition of an extra-chromosome [47]  
e.g. trisomy 21 or Mongolism or Down syndrome  
i.e. 3 copies of a chromosome instead of 2 in a pair.

2. **Monosomy:**  $2n-1$  e' missing of one chromosome [45]  
e.g. Turner syndrome (1 copy instead of 2 in a pair).

## Causes of an euploidy:

1. **Simple loss** [Anaphase lag]

failure of a chromosome to align during metaphase or lag to move in anaphase

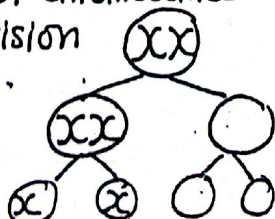
2. **Failure of duplication:** of a chromatid in S-stage.

3. **Non-disjunction:** types

(a) **Primary**

= failure of separation of chromosomes  
- during 1st meiotic division

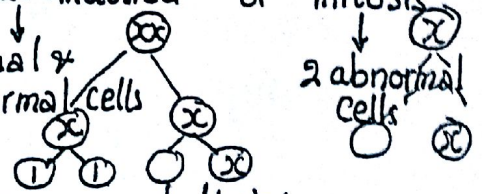
→ 4 abnormal cells



(b) **Secondary**

= failure of separation of chromatids  
- during 2nd meiotic or mitosis

2 normal &  
2 abnormal cells



(c) **Mosaic** if non disjunction occurs after many normal divisions →  
Cells e' more than Karyotype: some e' 46, others e' 45 or 47.



## Numerical Aberrations in Autosomes

### Down Syndrome = Mongolism = Trisomy 21

- A child e' 47 chromosomes, the extra-chromosome is similar to pair N<sup>o</sup> 21 i.e. each cell has 3 chromosomes e' the criteria of chromosome 21.
- Due to → Non-disjunction of chromosome 21
- Have mongol Features: mental retardation, hypotonia, cardiac abnormality, small genital organs, lateral upward sloping eyes, small ears, short broad nose, neck & hands.
- N.B. the older the woman at conception, the greater the risk of a child e' Down Syndrome

## Numerical Aberrations in Sex Chromosomes

Cause: Non-disjunction in 1<sup>st</sup> meiotic division of 1<sup>st</sup> Oocyte. the produced ovum contains XX or no X (O).

### 1] Klinefelter's Syndrome (47XXY) = [Trisomy of sex chr.]

- ♂ e' additional X-chromosome → So, have +ve Barr body
- due to non-disjunction of the X-chromosome in the 1<sup>st</sup> meiotic division in the Oocyte & the ovum e' 2X - " is fertilized e' Y-sperm.
- Features: mentally retarded ♂: tall child e' small testes, large breasts & widely separated nipples.

### 2] Multiple X chromosome [47XXX] = trisomy of X-chromosome

- similar cause as Klinefelter but the ovum is fertilized e' sperm e' X-chr
- ♀ e' additional X chromosome so - Have 2 barr bodies.
- Features: ♀ e' delayed language development, motor coordination problems, auditory disorders, accelerated growth until puberty.

### 3] Turner's Syndrome [45XO] = monosomy of X-chromosome.

- due to non-disjunction of the X-chromosomes during 1<sup>st</sup> meiotic division of oocyte the ovum e' no X chrom. is fertilized e' X sperm → 45 XO(-) →
- ♀ e' missing X " → -ve Barr body
- Clinically: short ♀ e' mental retardation, undeveloped ovaries & ext. genitalia, 1<sup>st</sup> amenorrhea + edema of limbs.



# Structural Aberrations (Mutation)

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They are mostly due to: viruses, exposure to radiation, drugs & insecticides  
If the chromosome has its normal genetic information → balanced aberration.  
If there is additional or missing " " → unbalanced " (affected phenotype)

## Types:

1. Breaks: rapidly heal by reunion of the sticky ends of the chromosomes.

2. Deletion: = loss of fragmented part of a chromosome; 3 types:

a. Terminal: loss of a segment from one end by a single break.

b. Interstitial: loss of a segment bet. 2 breaks e.g.

e.g. Wolf Syndrome: deletion of short arm of chromosome No 4.

Cri du chat " : " " " " " " " 5.  
(cry like cat)

c. Ring chromosome: 2 breaks, loss of fragments & reunion in a ring form.

3. Duplication = Addition:

the addition of extra piece to a homologous chromosome mostly due to unequal crossing over of homologous chromosomes → double the dose of genes on a chromosome i.e. 2 copies of the same gene on the same chromosome.

4. Inversion:

2 breaks in a chromosome & the broken segment rejoin its place but in an inverted form. 2 types:

a. Pericentric: the break is on either side of the centromere.

b. Paracentric: the break is on one side " " " "

5. Translocation:

= transfer of a chromosomal segment to a non-homologous chromosome.

2 types:

a. Robertsonian translocation [centric fusion]:

in acrocentric chromosomes 21 & 14: by fusion of the long arms of chromosomes 21 & 14 → t-chromosome. The short arms of both

" are lost (insignificant). It occurs in 3.4% of cases of Down Syndrome.

N.B. If a parent is a carrier of chromosome 21 translocation, the risk of having a child e! Down Syndrome is as high as 100%



Reciprocal translocation:

Exchange of segment bet. non homologous chromosomes - 12 -  
It is balanced, since no genes are lost or added.

Philadelphia Chromosome:

= reciprocal translocation bet chromosome 22 & chromosome 9  
It is diagnostic for chronic myeloid leukemia.

## 6 - Isochromosomes:

- transverse instead of longitudinal division of the centromere
- during anaphase of mitosis
- results in 2 non-similar chromatids.

→ 2 " " chromosomes: 1 e' 2 long arms  
1 e' " short "

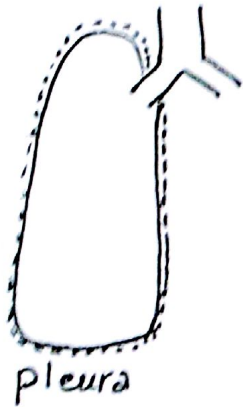
- It occurs in submetacentric chromosomes.



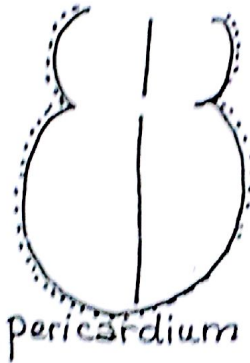
# Epithelial Tissue

## General Characteristics:

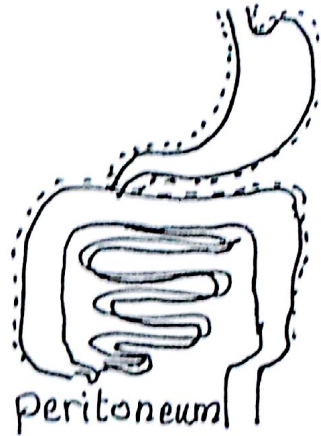
1. Origin: either ectodermal [e.g. skin], mesodermal [serous membrane] or endodermal [GIT].
2. Formed of crowded cells with minimal intercellular space.
3. Cells rest on a basement membrane. It may be clear or non-clear
4. Avascular: blood vessels & lymph vessels can not penetrate it but nerves can. [receives nutrition by diffusion from underlying c.t.]
5. It either covers surfaces or line cavities.
6. It may modify to: form secretion Glandular epith.
7. " " " " act as receptor neuro-epith. or
8. " " " " contract myo-epith.
9. have high power of regeneration.



pleura



pericardium



peritoneum

## Classification of epith:

1. Surface epith.: cover surface or line cavity.
2. Glandular epith. → secretion.
3. Neuro-epith. → sensation.
4. Myo-epith. → contraction.

### 1. Surface Epith

1. Simple epith  
(1 layer)

2. Stratified epith.  
(> 1 layer)

N.B.: Epith - metaplasia = transformation of epith from one type to another under abnormal condition.  
Eg:- epith of Bronchi (ps shed cell)  $\xrightarrow{\text{by smoking}}$  St. Sq.



# Simple Epithelium

formed of 1 layer of cells & subdivided according to shape of cells into:

## 1) Simple Squamous epith.

1 layer of flat cells & flat nuclei

Sites & functions:

1. Heart & blood vessels → smooth surface.

It is called endothelium.

2. Lung alveoli → thin surface for easy exchange of gases. It is called pneumocytes.

3. Serous membranes: Pleura, pericardium, peritoneum → smooth surface for easy movement. It is called mesothelium.

4. Bowman's Capsule of kidney → easy filtration.

## 2) Simple Cubical Epith.

1 layer of cubical cells with central rounded nuclei.

Function: Secretion & reabsorption.

Sites:

1. lining acini & small ducts of all exocrine glands e.g. (salivary)
2. Thyroid follicles.
3. Kidney tubules (have microvilli) for reabsorption.

## 3) Simple Columnar Epith.

1 layer of tall columnar cells & basal oval nuclei.

Function: Secretion & absorption:

Sites: GIT.

1. Stomach → secretion.
  2. Intestine → absorption
  3. Main pancreatic duct, Common bile duct & gall bladder
- (N.B) Goblet cells: modified col. cells = cub-shaped secrete mucous. present in small & large intestine & resp. tract.

## 4) Simple Columnar Ciliated Epith.

1 layer of columnar cells. The free surface have cilia.

Functions: cilia push fluids or particles in one direction.

Sites:

♀ Genital tract: Uterus & Fallopian tube (move the ova).  
lung bronchioles: (push mucous)

## 5) Pseudo-stratified Columnar Epith.

1 layer of columnar cell crowded over each other.

All cells rest on the basement membrane but some cells fail to reach the surface. Nuclei are present at different levels giving the appearance of many layers (stratified). 2 types:

### a) Pseudo-stratified columnar ciliated epith.

i) Non-motile cilia & goblet cells:

lining upper respiratory tract e.g. nose, trachea & bronchi. It is called respiratory epithelium.

ii) Non-motile cilia (stereocilia) = not

= not true cilia = long microvilli

e.g. in epididymis.

### b) Pseudo-stratified Columnar Non-ciliated epith.

In ♂ genital tract.

e.g. Vas deferens

membranous part of ♂ urethra.



# Stratified Epithelium

Formed of 1 layer of cells: It's main function is protection. Classified according to the shape of superficial cells into

## 1. Stratified Squamous epith.

- Formed of 5-30 layers (thickest type)
- Cells rest on a clear & wavy basement memb.
- The basal layer:
- Columnar cells e' basal oval nucleus.
- From this layer, the other cells originate
- The intermediate layers:
- polygonal cells e' central rounded nuclei e'
- minimal intercellular spaces & joined by desmosomes.
- Cells become smaller towards the surface (less nourished).
- The superficial layer:
- Flat squamous cells e' flat nuclei.
- 2 types:

### (a) Non-Keratinized: (wet)

the superficial cells are living e' no Keratin.

Sites:

1. Oral cavity: lip & tongue (mouth)
2. Oesophagus.
3. Cornea.
4. anal canal
5. Tip of urethra
6. Vagina.

### (b) Keratinized: (dry)

the superficial cells die, lose their nuclei & form Keratin scales

Sites: (dry & exposed surfaces)

1. Epidermis of skin.
2. Openings upon skin

ext. ear  
ext. nose  
anus.

## 3. Stratified Cubical epith.

few number of layers & the superficial cells are cubical. In ducts of sweat glands (formed of 2 layers of cubical cells)

## 2. Transitional Epith. (str. cuboidal)

- Formed of 6-8 layers: (in empty bladder)
- Cells rest on non-clear & non-wavy basement memb.
- The basal layer: high cuboidal cells e' central rounded nucleus
- The intermediate layers = polygonal cells e' central rounded nuclei e' wide intercellular spaces w' contain mucous like substance to allow gliding of cells over each other.
- The superficial layer: large cuboidal cells e' upper convex surface. [dome cells] & may be binucleated
- It is covered e' mucous to protect against action of urine
- (N.B) Absence of desmosomes & presence of wide intercellular spaces filled e' mucous like substance help gliding of cells over each other during distention of the bladder & epith becomes thinner (2-3 layers. During full distention, cells may become flattened i.e. changeable).

### Sites: Urinary tract: [uro epith.]

e.g. renal pelvis, ureter & urinary bladder.

## 4. Stratified Columnar epith.

Similar to stratified squamous but: Fewer No. of layers & superficial cells are columnar

2 types:

Non-ciliated in

- recto-anal junction
- penile part of urethra
- large ducts of glands

Ciliated.

rare in foetal

Oesophagus



## II Glandular Epithelium

-4-

f.: epithelial cells specialized to produce secretion.

According to presence or absence of ducts, glands are classified into 3 types:

| A. Exocrine glands:                                                                         | B. endocrine glands                                                                               | C. Mixed glands.                                       |
|---------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|--------------------------------------------------------|
| Have secretory unit & ducts to carry the secretion to the surface.<br>e.g. Salivary glands. | groups of cells but no ducts. & cells pour the hormone directly into blood<br>e.g. thyroid gland. | have both exocrine & endocrine parts<br>e.g. pancreas. |

### • Classification of Exocrine Glands:

#### 1. According to No. of cells:

- a. Unicellular glands: e.g. goblet cells.
- b. Multicellular " : all other glands e.g. salivary glands.

#### 2. According to Mode of secretion: [Mechanism].

i.e according to the changes in the secretory cells.

- a. Merocrine: no change, secretion passes by exocytosis e.g. salivary glands.
- b. Apocrine: the apex of the cell detach & come out e' the secretion.  
e.g. mammary gland & axillary sweat glands.
- c. Holocrine: the whole cell is destroyed & lost e' the secretion.  
e.g. sebaceous gland.

#### 3. According to the Nature [Kind] of Secretion:

- a. Watery secretion: e.g. sweat glands.
- b. Serous glands: Watery secretion containing enzymes e.g. Parotid & Pancreas
- c. Mucous glands: e.g. goblet cells.
- d. Muco-serous gls: e.g. submandibular & sublingual glands.
- e. Fatty secretion: e.g. sebaceous glands.
- f. Waxy glands: e.g. glands of external ear.
- e. Cellular " : → cells e.g. Testis (sperms) & Ovary (ova).

#### 4. According to function:

- a. Secretory: secrete useful substance e.g. salivary glands
- b. Excretory: excrete waste products e.g. kidney & sweat glands.



According to the shape of the secretory unit:

tubular, alveolar or tubulo-alveolar.

6. According to branching of the ducts:

a. Simple: have single non-branching duct

b. Simple branched: the duct is not branched but acini are branched

c. Compound: the ducts are branched like a tree.

Examples of exocrine glands according to shape of acini & branching of the ducts.

a) Tubular:

• Simple tubular  
e.g. intestinal gl.  
(crypts)

• Simple branched tubular:  
e.g. Fundic gland of Stomach

• Simple Coiled tubular  
e.g. Sweat gl.

• Compound tubular:  
e.g. Liver  
Kidney  
testis

b) Alveolar:

• Simple Alveolar  
e.g. Sebaceous gland

• Simple branched alveolar  
e.g. Sebaceous gls.

• Compound alveolar  
e.g. Mammary gland

c) Tubulo-alveolar:

• Simple tubuloalveolar  
not in Man.

• Simple branched tubulo-alveolar  
e.g. minor salivary glands of mouth cavity.

• Compound tubulo-alveolar  
e.g. Main salivary gls.  
(parotid) + pancreas  
+ prostate.



### III - Myoepithelium

- epithelial cells modified to contract.
- branched cells w/ many processes that contain contractile filament.
- they surround the acini of the glands, between the base of cells & the basement memb. When they contract they squeeze the acini so, discharge the secretion into the ducts. e.g. sweat glands, salivary gls. & mammary gland.

### IV Neuro-epithelium

- epithelial cells modified to act as receptors.
- formed of: sensory cells & supporting cells.

#### Sites :

1. Taste buds : in tongue : for taste.
2. Organ of Corti : in inner ear : for hearing .  

|                         |   |       |                    |
|-------------------------|---|-------|--------------------|
| <u>Crista ampularis</u> | } | " " " | : for equilibrium. |
| <u>Macula utriculi</u>  |   |       |                    |
| <u>" sacculi</u>        |   |       |                    |
3. Rods & Cones : in retina : for vision.



# Polarity & Memb. Specializations

## I. Lateral [Intercellular] Specializations

Epith. cells are linked by diff. types of junctions.

### 1] Tight [Occluding] Junctions

#### A. Zonula Occludens =

- The 2 adjacent cell membranes fuse completely at certain points where the intercellular space is (0).
- It completely encircles the apex of the cell like a belt.
- function: prevent passage of substances bet. the cells.

#### B. Fascia Occludens:

- Similar to Z.O. but not like a belt. It is a patchy fusion of the two cell membranes e.g. bet. endothelial cells.

### 2] Adherens Junctions [Zonula Adherens]:

- the 2 adjacent cell membs. are separated by a wide space (20 nm) filled w' adhesive (cell coat) material.
- At the cytoplasmic side, there is condensation of actin microfilaments.
- It encircles the cell like a belt.
- Function: fix adjacent cells to prevent their separation.

### 3] Macula Adherens = Desmosomes:

- the 2 adj. cell membs. are separated by a very wide space (30 nm) filled w' adhesive material. It does not encircle the cell but scattered as circular spots.
- the cytoplasmic side is thickened → attachment plates in w' tonofilam (intermediate) filaments are inserted & return back to cytoplasm → hair pin like loops
- It shows electron-dense line in the middle of the intercellular space.
- formed of transverse filaments = trans-membrane linkers.
- Present bet. epithelial cells esp. in strat. squamous epith.
- functions: strongest type that holds cells together & give support to surfaces subjected to mechanical stress & friction.

### (N.B.) Junctional Complex:

If more than 1 junction are present bet. adjacent cells e.g. Col. cells lining the small Intestine show Z. occludens at the apex followed by Z. adh. & desmosomes.



## Gap Junction: [Nexus] = Communicating Junction

-0-

the 2 adjacent cell membs. are separated by a very narrow gap (2 nm) but connected by narrow channels = 6 integral transmembr. ptns (hexameric) forming tubules called connexons.  
The joined connexons → nexus.

### Functions:

1. permit passage of ions & small molecules from one cell to the other.
2. passage of impulses bet. muscle cells e.g. cardiac & smooth muscles.

## II Basal Specializations

### 1. Hemidesmosomes:

- take the shape of  $\frac{1}{2}$  a desmosome.
- at basal part of basal cells.

Function: fix epith. to underlying b.m. & c.t.

### 2. Basement membrane:

- memb. beneath all epithelia, bet. epith. & c.t.
- L.M.: red line by (PAS) or brown by (Ag).

Maybe → Clear (thick) e.g. skin.

- non-clear (thin) e.g. transitional epith & capillaries.

- E.M.: 2 components:

A. Basal Lamina = Cell Coat = [epith. component]

→ lamina lucida = electron-lucent (clear) layer → glycoptn. of cell coat + laminin

→ lamina densa = electron-dense & more condensed " " " " " " collagen granules (type IV)

B. Reticular lamina = collagen of c.t. [c.t. component].

= fine collagen fibrils (type III) = reticular fibres + glycoptns.

Both layers are fixed to c.t. by collagen fibres type VII = anchoring fibres

### Functions:

1. Support epith & help to form sheets.

2. fix epith. to c.t.

3. help repair of epith.

4. act as a sieve to control passage of nutrients & ions e.g. Kidney caps, lung alveoli

### 3. Basal Infoldings:

In ion transporting cells e.g. Kidney tubules. the basal cell memb. shows invaginations + vertical mitochondria to give Energy for active transport of  $\text{Na}^+$



### III Apical Specializations

#### 1. Microvilli:

- finger like projections from the cell memb., shorter than cilia.
- L.M. = apical striated (brush) border.
- E.M. have a core of actin filaments inserted into a terminal web.  
the actin core maintain its shape & help shortening & elongation of microvilli.
- Functions: ↑↑ surface area for absorption up to 30 times e.g. small intestine  
kidney tubules

#### 2. Stereocilia = [non-motile cilia]

- Not true cilia but long microvilli.
- L.M. hair like processes from free surface of some cells.
- E.M. no microtubules (not cilia), their core have actin filaments.
- Function: help absorption in ♂ genital system e.g. epididymis.

#### 3. Cilia:

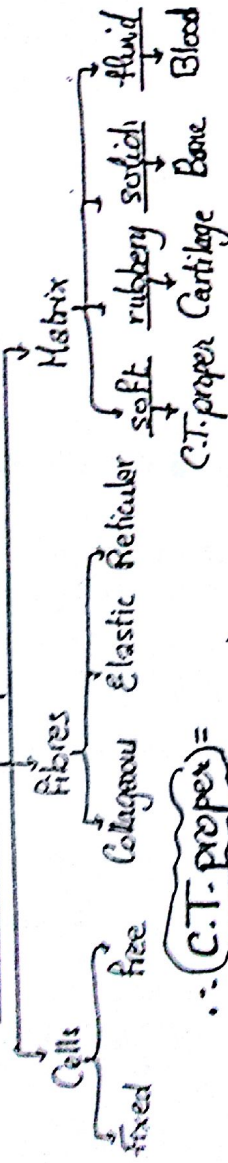
- L.M. hair like processes w arise from the free border of some cells.
- E.M. formed of a core of 20 microtubules arranged as 9 peripheral doublets & 2 central singlets called axoneme covered e' cell memb. & continuous e' the basal body.
- Functions:
  - their rhythmic beating push particles or fluids in one direction.
  - In cells lining upper respiratory tract e.g. trachea & bronchi, mucous traps dust & bacteria move it towards the throat to be coughed.
  - In cells lining Fallopian tube: transport the ovum towards the uterus.

#### 4. Flagella:

- Single extra long cilium that form the tail of sperm.
- Its whip like movement help to move sperms.



formed of 3 components:



Cells + Fibres + soft matrix

## C.T. Cells

**Fixed Cells:** stable population, produced & remain in c.t. & long lived:

(1) **UMC** = undifferentiated mesenchymal cell

**Site:** in c.t. of embryo (mesenchymal c.t.)  
in adults → around bl. capillaries (pericyte)

**L.M.:** Small branched stellate shaped cells.  
N. large, pale, oval e' clear nucleolus.  
C. pale basophilic

**E.M.:** Few organelles but many free ribosomes

**Functions:** Can differentiate into:  
1. Other c.t. cells  
2. bl. cells  
3. smooth muscles  
4. endothelial cells

## Reticular cells.

**Origin:** UMC.

**Site:** Stroma of different organs.

**L.M.:** small stellate shaped cell e' long processes.  
N.: central, rounded, pale e' prominent nucleolus.  
C.: pale basophilic.

**Functions:** processes joined by cell junctions.  
1. secrete reticular fibres  
2. supportive  
3. On need act as phagocytic cell  
4. Antigen presenting cell

## Characters of c.t.

1. mesodermal in origin
2. Cells are widely separated e' large amount of matrix
3. bl. vs, lymph us vane can penetrate it.
4. Connect, support & protect tissues & organs.

mesoderm → mesenchymal c.t. = UMCs + ground substances

## (3) Fibroblasts & Fibrocytes (build c.t.)

**Origin:** UMC & pericytes.

**Site:** in all types of c.t. [most common type].

**L.M.:** Flat (stellate) branched cell e' long processes.  
N. large, pale, oval e' prominent nucleolus.  
C. deeply basophilic.

**E.M.:** picture of ptn. forming cells:

N. Euchromatic nucleus e' prominent nucleolus  
C. many mit., rER, ribosomes, well developed G.A.

**Functions:** 1. Form c.t. matrix.  
2. " " fibres.

3. Healing of wounds.

4. secrete growth factors for growth & differentiation of cells.

## Fibrocyte = Old Fibroblast (inactive)

- Spindle shaped e' few processes
- small dark Nucleus & pale basophilic cytopl.
- Fewer rER, N. e' condensed chromatin
- F: maintenance of c.t. Active during healing of wounds.



(6) Fat Cells [Adipocyte]

Origin: LMC  $\rightarrow$  lipoblast  $\rightarrow$  lipocyte

### A. Unilocular Fat Cell

- Site: - white adipose c.t.

- L.M: Large oval cell (50-150  $\mu\text{m}$ )  
 e' large globule of fat surrounded e'  
 small rim of cytoplasm.  
 N. flat & peripheral.

by  $H \times E$ : Fat dissolves  $\rightarrow$  empty space  $\rightarrow$  signet ring appearance  
by Sudan III  $\rightarrow$  Orange.

E.M. few <sup>filamentous</sup> mit., many free ribosomes + S-ER  
dense inclusion filling the cell.

Functions :

1. storage of fat.
2. Heat insulator
3. support organs e.g. Kidney

N.B. Fat cells do not divide but long lived.

### B. Multilocular fat cell

- Brown adipose c.t.

- Small rounded cell & small fat droplets & central rounded N.

- No signet ring appearance.

E.M. many <sup>spherical</sup> mitochondria contain brown cytochrome pigment + few free ribosomes

Function: Heat generator.

(7) Fixed Macrophages [Histocytes]: -

Origin: monocyte.

Site: Scattered in c.t. attached to collagen fibres.

L.M. large branched cell e' pseudopodia, so have variable shapes

N: small, dark & kidney shaped.

C: Non-clear, pale basophilic

Special stain: vital stain as trypan blue or Indian ink.  
where the stain is phagocytosed by the cell.

E.M. - Irregular surface due to pseudopodia.

- Few rER, well developed **G.A.** many lysosomes  $\rightarrow$  phagocytosed particles + residual bodies.

## Functions :

1. Phagocytosis → digest microorganisms.
2. Fuse → multinucleated **foreign body giant cells** to phagocytose large foreign bodies.
3. Clean wounds from dead cells [debris].
4. destruction of old RBCs in liver & spleen.
5. Antigen presenting cells i.e. trap & partially digest the antigen to present it to lymphocytes.
6. secrete enzs e.g. collagenase & cytokines [important in defence & repair].



## II Free C.T. cells: motile, migrate from blood, belong to immune system, short lived & continuously rep.

| (1) Plasma Cell                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | (2) Mast Cell                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | (3) Free Macrophages                                                            | [4] Bl. leucocytes                                                 |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------|--------------------------------------------------------------------|
| <p>Origin: <math>\beta</math>-lymphocytes <math>\rightarrow</math> plasmablasts <math>\rightarrow</math> plasma cells.</p> <p>Site: - lymphatic tissue.</p> <p>L.M. - large Oval cell (20 <math>\mu</math>m)</p> <p>N. eccentric rounded e' Cart. wheel or clock face appearance</p> <p>C. deeply basophilic e' unstained area near the nucleus = -ve Golgi image.</p> <p>- may contain acidophilic granules = Russell bodies = accumulations of defective products of antibody synthesis.</p> <p>E.M. of ptn. secreting cells i.e. mit., many cisternae of rER, well developed G.A.</p> <p>N. radiating chromatin masses under the nuclear memb.</p> <p>Function: form &amp; secrete antibodies</p> | <p>- UMC</p> <p><math>\rightarrow</math> around bl. capillaries &amp; under epith. of respiratory &amp; digestive tracts.</p> <p>- Oval Cell e'</p> <p>- N: central &amp; rounded.</p> <p>C. have basophilic granules w are metachromatically stained e' toluidine blue <math>\rightarrow</math> purple or red color</p> <p>E.M. mit, rER, G.A. + memb. bound dense granules.</p> <p>Functions:</p> <ol style="list-style-type: none"> <li>1. Secrete Heparin (anticoagulant)</li> <li>2. Secrete Histamine <math>\rightarrow</math> Vasodilation that initiates allergy.</li> <li>3. Secrete Eosinophil chemotactic factor w attracts eosinophils to site of allergy</li> <li>4. Secrete leukotrienes: <math>\rightarrow</math> contraction of smooth muscles of the bronchial tree <math>\rightarrow</math> bronchial asthma.</li> </ol> | <p>blood monocytes w migrate to c.t. &amp;</p> <p>Same as Fixed macrophages</p> | <p>migrated from blood through capillaries &amp; small venules</p> |



**Lipocytes:** secrete leptin hormone to regulate appetite & the amount of fat in the body.

**In multilocular fat cells:** the mitochondria contain a protein called thermogenin (a unique marker for these cells) that  $\uparrow$  heat production.

**C.T. cells** are classified according to **function** into:

1. Undifferentiated cells = UMCs + pericytes
2. C.T. forming cells = fibroblasts, fibrocytes + reticular cells
3. Fat storing cells = unilocular & multilocular fat cells.
4. Cells responsible for immunity & defense = plasma cells, mast cells, leucocytes + macrophages [fixed & free].

**Extracellular Matrix** = Ground Substance + tissue fluid

**def.** Jelly like, transparent substance formed by fibroblasts.

**formed of:**

① **Glycosaminoglycans = GAGs**

= polysaccharides = repeated disaccharides e.g.  $\left[ \begin{array}{l} \text{chondroitin sulphate} \\ \text{heparan} \\ \text{Hyaluronic A} \end{array} \right] +$

② **Proteoglycans:**

90-95% CHO linked to ptn. molecules (10%)

③ **Glycoproteins:**

large ptn. molecules (90%) linked to <sup>repeated</sup> monosaccharides  $\rightarrow$  polysaccharides

**Tissue Fluid:**

similar to plasma (- plasma ptns) derived from capillaries (through pores)

**Stain:** Ag  $\rightarrow$  brown. Toluidine blue  $\rightarrow$  purple [metachromatic stain].

**Functions:**

1. Allow passage of nutrients, & waste products bet. cells & blood.
2. physical barrier against spread of microorganisms.

**Edema** = accumulation of excess fluid in the extracellular space

**Causes:** 1.  $\uparrow$  capillary permeability.

2.  $\downarrow$  venous flow.

3. lymphatic obstruction.



# C.T. fibres

| White Collagenous fs                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Yellow Elastic fs.                                                                                                                                                                                                                                                                                                       | Reticular fibres                                                                                                                                                                                                                                                                                 |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p><b>L.M.</b> - Wavy branching bundles formed of parallel non-branching fibres.</p> <p>- Colourless, appear white when condensed.</p> <p><b>Stains:</b> H+E: acidophilic → pink (e' eosin)<br/>Mallory → blue<br/>Van Geison → red</p> <p><b>Structure:</b> procollagen → procollagen → tropocollagen = 3 polypeptide chains intertwined in triple helix. tropocollagen polymerize → fibrils → fibres → bundles</p> <p><b>E.M.</b> collagen fibrils have t.v. striations with dark bands that react more intensely e' the lead stain used in EM than do the light bands.</p> | <p>- thin, single fibres</p> <p>- branching</p> <p>- appear yellow in fresh section</p> <p>- H+E → pink</p> <p>- Orcein → brown</p> <p>- Von Geison → yellow</p> <p>2 types of ptn → elastin microfibrillar glycoprotein.</p> <p>core of elastin surrounded by microfibrillar ptn.</p> <p>No fibrils, No periodicity</p> | <p>- Very thin fibres w branch &amp; anastomose to form reticulum.</p> <p>- Ag → black [argyrophilic]</p> <p>- PAS → purple (high CHO content)</p> <p>- Collagen type III thin fibres of tropocollagen bound by glycoptn. molecules (contain 6-12% hexose) compared to 1% in collagen type I</p> |
| <p><b>Character:</b> strong, resist stretch, flexible.</p> <p>- by boiling → gelatin</p> <p>- destroyed by acids &amp; alkalis</p> <p>- digested by pepsin &amp; trypsin.</p> <p>- tanning → leather</p>                                                                                                                                                                                                                                                                                                                                                                      | <p>- stretch &amp; recoil.</p> <p>- resist boiling.</p> <p>- resist chemicals.</p> <p>- digested by pancreatic elastase</p>                                                                                                                                                                                              | <p>Supportive stroma. allows motility of cells in b.m, lymph Node &amp; spleen.</p>                                                                                                                                                                                                              |
| <p><b>Function:</b> give tissues strength &amp; resist stretching</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | <p>- give tissues elasticity.</p>                                                                                                                                                                                                                                                                                        | <p>Fibroblasts, reticular cells smooth muscles.</p>                                                                                                                                                                                                                                              |
| <p><b>Formed by:</b> Fibroblasts, chondroblasts (in cartilage) Osteoblasts &amp; odontoblasts (in teeth) (in bone)</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                        | <p>Fibroblasts, chondroblasts in elastic cart. smooth muscles in elastic arteries</p>                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                                                                  |



Collagen is the most abundant ptn. in the body

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Types of collagen: >20 type

| Type                         | Main Sites                                          | Cell of Origin                                     |
|------------------------------|-----------------------------------------------------|----------------------------------------------------|
| Type I                       | C.T. proper, bones, tendons + capsules of organs    | - Fibroblast + Osteoblasts                         |
| Type II                      | Cartilage + vitreous body of eye                    | - Chondroblasts + Chondrocytes.                    |
| Type III<br>reticular fibres | loose c.t. Stroma of organs<br>wall of bl. vessels. | - Fibroblasts, reticular cells + smooth ms. cells. |
| Type IV                      | - basal lamina of epith. & endoth.                  | - Epithelial cells.                                |
| Type V                       | Ext. lamina of smooth & skeletal ms.                | - Fibroblasts.<br>- muscle cells.                  |
| Type VI                      | - Associated w' type I & III                        | - Fibroblasts.                                     |
| Type VII<br>anchoring fibres | In skin in dermo-epidermal junctions.               | - Fibroblasts                                      |

**Scurvy:** vit. C. deficiency → defective collagen synthesis  
characterized by: bleeding gums & loss of teeth & unhealed wounds

### Types of c.t. Proper

#### Loose

1. loose areolar c.t.
2. Adipose c.t.
3. Reticular c.t.
4. Mucoid c.t.

#### Dense

1. White fibrous c.t.
2. Yellow elastic c.t.



## A. loose C.T.

### (1) Loose [Areolar] C.T.

- The most common type :
- Structure → all cells mainly: Fibroblasts, fat cells, mast cells + macrophages  
                   → all fibres " collagenous + abundant matrix.
- Characters: - contain cavities (areolae) w<sup>h</sup> can accomodate fluids & gases.  
                   - well vascularised delicate & flexible.
- Functions: 1. binds organs & tissues.  
                   2. exchange of nutrients e<sup>l</sup> bl. vs.  
                   3. limits spread of infection.

Sites: all over the body except the brain.

1. Subcutaneous (dermis of skin).
2. Submucosa.
3. Serous membranes.
4. around blood vessels & nerves.

## 2. Adipose c.t.

- Similar to areolar c.t. but fat cells predominate.
- Cells: large No of fat cells e<sup>l</sup> few fibroblasts & mast cells in between.
- Fibres: collagenous & elastic fibres form septa bet. lobules of fat cells.

| Types: A. White Adipose c.t.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | B. Brown adipose c.t.                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p><u>characters</u>:</p> <ul style="list-style-type: none"> <li>have Unilocular fat cells</li> <li>Non pigmented</li> <li>poor in blood supply</li> <li>affected by diet &amp; hormones</li> </ul> <p><u>Functions</u>:</p> <ol style="list-style-type: none"> <li>1. Storage of fat.</li> <li>2. support organs e.g. kidney</li> <li>3. heat insulation</li> <li>4. give skin its normal contour.</li> </ol> <p><u>Sites</u>:</p> <ol style="list-style-type: none"> <li>1. Under skin esp. ♀ e.g.: mammary gland &amp; gluteal region</li> <li>2. Abdominal wall &amp; mesentery.</li> <li>3. Around Kidney &amp; bl. vs.</li> </ol> | <p>→ multilocular fat cells.</p> <ul style="list-style-type: none"> <li>→ brown due to cytochrome in mit.</li> <li>→ rich in bl. supply.</li> <li>→ not affected by starvation.</li> </ul> <p><u>Functions</u>:</p> <ul style="list-style-type: none"> <li>- heat generator for newborns.</li> </ul> <p><u>Sites</u>:</p> <ul style="list-style-type: none"> <li>• In Embryo &amp; newborns:</li> <li>bet. scapulae, axilla, mediastinum &amp; gradually replaced by white fat.</li> </ul> |



### 3] Mucoid C.T.

Embryonic type in w matrix predominate

Formed of:

1. Cells: UMC or young Fibroblasts e' multiple connected processes
2. Fibres: fine collagenous & reticular fs.
3. Matrix: soft, jelly-like rich in mucus & hyaluronic acid.

Sites:

1. Umbilical Cord [Wharton's Jelly]
2. Vitreous humor of eye.
3. Pulp of teeth.

### 4] Reticular C.T.

Formed of:

1. Cells: reticular cells joined by their long processes
2. Fibres: fine reticular fibres together e' the cells form reticulum.

Sites:

Stroma of all organs  
↳ all glands.

Stain: Ag → brown to black

## B. Dense types of C.T.

### 5] White Fibrous C.T.

Very dense e' predominant collagenous fibres e' few cells.

Formed of: white collagenous bundles separated by fibroblasts (tendon cells) & small amount of matrix

Characters: white in fresh section.

types: according to arrangement of collagenous bundles: 2 types:

| Regular                                                                                                                                                                                                                                                                                                                                                                                                       | Irregular                                                                                                                                                                                                                                                                                                                                       |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"><li>- the bundles are regular &amp; parallel</li><li>- Fibroblasts are arranged in rows (tendon cells) in bet. collagen bundles</li><li>- very little amount of matrix</li><li>- <u>Function</u>: withstand stretch in 1 direction</li><li>- <u>Sites</u>:<ol style="list-style-type: none"><li>1. Cornea of eye</li><li>2. Tendons of skeletal muscles</li></ol></li></ul> | <ul style="list-style-type: none"><li>- Collagen bundles are irregular</li><li>- withstand stretch in diff. directions</li><li>- <u>Sites</u>:<ol style="list-style-type: none"><li>1. Sclera of eye</li><li>2. ligaments</li><li>3. capsule of organs</li><li>4. perichondrium &amp; periosteum.</li><li>5. Dermis of skin</li></ol></li></ul> |



## 6. Yellow Elastic C.T.

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dense type & predominant elastic fibres

formed of: fibres: regular parallel elastic fs.

Cells: few fibroblasts & fibrocytes.

Characters: yellow in fresh section.

Stain & Orcein → brown.

function :- form elastic membranes  
- have great elastic power (rubber like)

Sites:

1. **Aorta** & large arteries.
2. **Bronchi**, bronchioles & around alveoli
3. **Ligaments**: ligamentum nuchae  
ligamentum flavum  
suspensory lig. of penis
4. **Vocal Cords**.



# Cartilage

2014

def: It is a type of c.t. in w the matrix is rubbery to bear mechanical stress.

## Characters:

1. arise from UMCs.
2. the matrix is rubbery but flexible.
3. Cells are widely separated by large amount of intercellular matrix.
4. It is avascular & no lymph vessels & no nerves.
5. Nourished by diffusion of  $O_2$  & nutrients from c.t. (perichondrium) or synovial fluid in joints.

## Structure:

- Cells = Chondroblasts & chondrocytes.
- Fibres = Collagenous & elastic fibres (in diff. proportions)
- matrix = abundant & firm (rubbery)

## 3 Types:

### 1. Hyaline Cartilage

the most common type. It is translucent (glassy) in fresh section.

## Structure:

### A. Perichondrium

- dense fibrous c.t. that covers the cartilage except at articular surface of joint.
- formed of 2 layers:
  1. Outer Fibrous Layer = Collagenous bundles (type I) + fibroblasts + bl. vessels + nerves.
  2. Inner Chondrogenic L. (Cellular L.) = Chondroblasts (Chondrogenic cells  $\rightarrow$  chondrocytes)
- Functions:

1. Nutrition of the non-vascular cartilage (by diffusion)
2. Give muscle attachment.
3. Formation of new cartilage during growth.

### B. Cartilage Cells:

#### 1. Chondroblasts: [young or immature chondrocytes]

Origin: UMC w withdraw their processes, proliferate & give chondroblasts w start to secrete matrix.

Site: inner layer of perichondrium

L.M.: small oval cell & pale oval nucleus & clear nucleolus & deeply basophilic cytoplasm. it can divide.

E.M.: pln. forming cell i.e. Euchromatic nucleus, many mit., well developed G.A. + r.ER.

- Functions:
1. Form Collagen [type II].
  2. Form cartilage matrix.
  3. change into chondrocytes.
  4. growth of cartilage [appositional]

#### 2. Chondrocytes:

Origin: Chondroblasts when surrounded by the matrix (imprisoned)

Site: present inside lacunae & surrounded by capsule of condensed matrix.

L.M. Cells have pale basophilic cytoplasm (rich in alcunonem & fat w dissolve during preparation) & central rounded nucleus.

N.B during preparation, cells shrink leaving space called lacuna (not present during life)



- 2
- the superficial cells are small, oval, present singly inside their lacunae & // to surface
  - the deep cells (older): are large, rounded or triangular either single or divide to give groups of 2, 4 or 8 cells (isogenous groups) in 2-4 lacunae  
→ cell nest.

E.M. mit, G.A., rER + fat droplets + glycogen granules.

Function: maintain matrix by secretion of its components.

## C. Fibres:

Collagen fibres (type II) embedded in the matrix w appears homogenous & transparent they cannot be seen by L.M. because: 1. they are very thin  
2. they have the same refractive index as the matrix.

(N.B.) can only be seen after digestion of the matrix by enzymes

## D. Matrix (ground Sub.):

- 'rubbery', homogenous (transparent) & deeply basophilic (sulfated GAGs).
- produced by chondroblasts & chondrocytes.
- consists of: proteoglycans + glycoproteins + H<sub>2</sub>O
- stains metachromatically & basic stains.

## Sites:

1. Costal Cartilage.
2. Upper respiratory passages e.g. nose, larynx, trachea & bronchi.
3. Articular surface of joints.
4. Foetal skeleton.
5. Epiphyseal plate.

## 2. Yellow Elastic Cartilage

Structure: Similar to hyaline cartilage but the matrix is rich in branching yellow elastic fibres & few collagenous fibres (type II). It is yellow in fresh section & more flexible. It is covered & perichondrium. Chondrocytes are single or form small cell nests (2 cell isogenous groups)

Function: Very flexible, recovers its shape after being deformed.

Sites: (where support & flexibility are needed) 4E:

1. Ear pinna
2. Ext. auditory canal.
3. Eustachian tube.
4. Epiglottis & some laryngeal cartilages.

## 3. White Fibro-Cartilage

Structure:

- It has no perichondrium.
- Formed of: parallel collagenous bundles (type I) separated by chondrocytes in rows embedded in little amount of matrix.
- has intermediate characters bet. hyaline cartilage & dense regular white fibrous t.
- Functions:
  1. strong tough type w resist stretch.
  2. Imp. in bone to bone attachment & limited movement.



- Sites:

1. Intervertebral disc.
2. Symphysis pubis.
3. lip of acetabulum (hip) & glenoid cavity (shoulder) joints.
4. Sternoclavicular & mandibular joints.
5. Semilunar cartilage of knee joints.

### Intervertebral disc

- bet. adjacent vertebrae
- Formed of
  - Out. fibrous ring [annulus fibrosus] = White fibro-cartilage.
  - Inn. soft mass [nucleus pulposus] = collagen type II.

**Disc Prolapse:** Herniation of nucleus pulposus from annulus fibrosus → compress nerve roots → severe pain.

### Growth of Cartilage

#### 1. Appositional Growth: (exogenous)

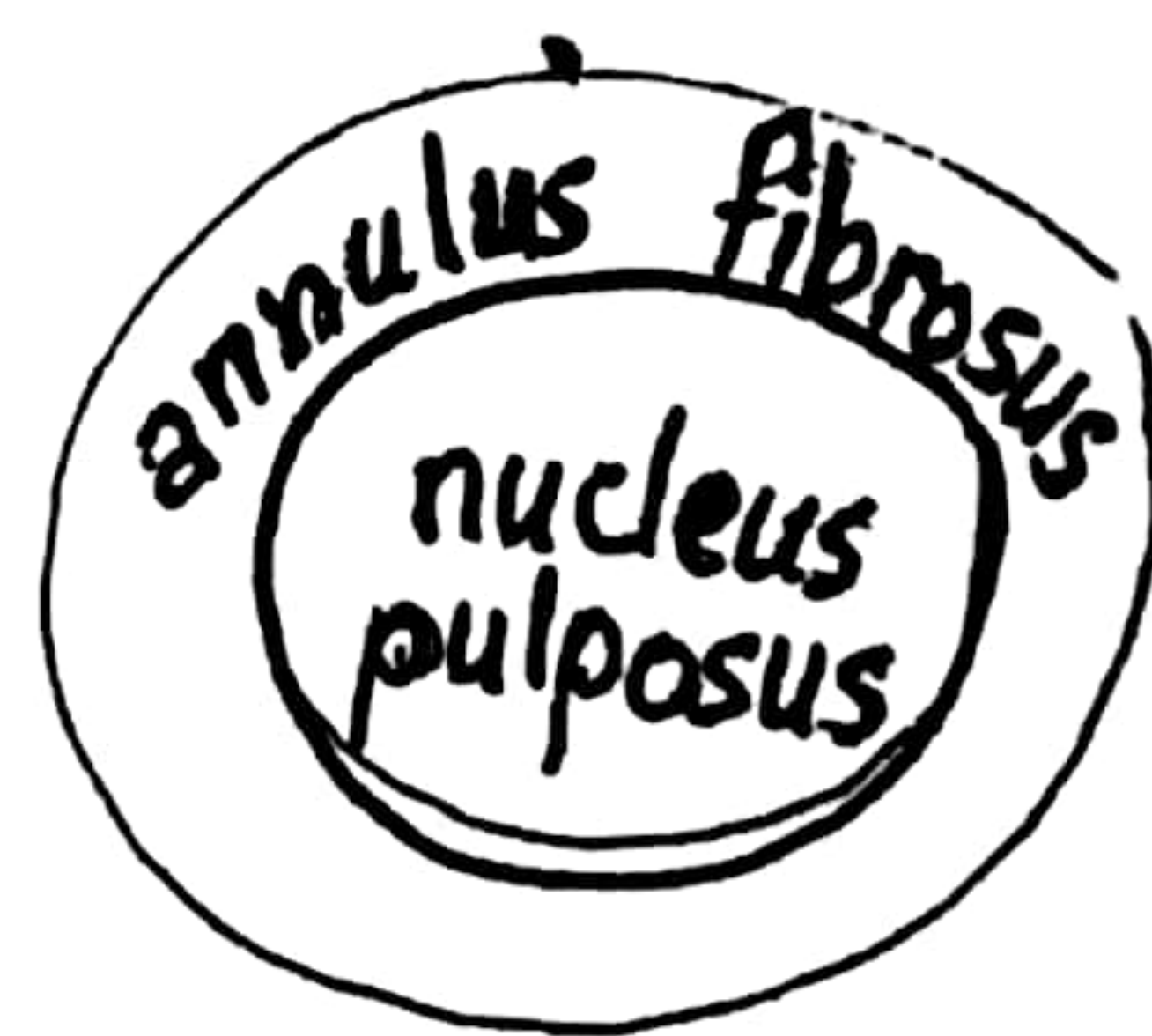
Addition of new layers of cartilage to the surface by chondroblasts in the inner chondrogenic layer of perichondrium

#### 2. Interstitial Growth:

growth from inside by proliferation of young chondrocytes w divide & form matrix around them.

### Functions of Cartilage

1. Keep patent airways.
2. Support soft tissues & give some flexibility & weight bearing
3. Shock absorbing.
4. Smooth & easy (sliding) movement of joints.
5. development & growth of bone (before & after birth)





# Bone

2014

(1)

**def.:** A type of c.t. in w the matrix is hard & vascular.

**Structure:** Cells  $\nwarrow$  + Fibres [collagen type I] + solid matrix  
+ periosteum & endosteum [rich in Ca & phosphorus]

## Functions:

1. Form adult skeleton [body support]
3. protect vital organs e.g. brain, b.m.
4. reservoir for Ca

**Shapes of bone:** Anatomical classification

1. long bones.
2. short bones.
3. flat bones
4. Irregular bones

**Types of bone:** histological classification:

1. Compact (regular) bone
2. Spongy (irregular) bone.

## Structure of Bone

### Bone Matrix

matrix  
cells

periosteum, endosteum

lamellae of calcified collagenous bundles separated by calcified ground substance.

**1. Organic Component: 35%:** secreted by bone cells

- collagen type I: so, the matrix is acidophilic.

- ground substance = proteoglycans [GAGs] & glycoproteins.

**2. Inorganic Component: 65%:**

Ca phosphate & carbonate. Ca salts appear as crystals on the surface of collagen bundles & in ground substance.

## 2 methods for preparing bone sections:

**1. Decalcified compact bone:**

Ca is removed (dissolved) by nitric A. 10%  $\rightarrow$  soft tissue w can be cut & stained as usual. It demonstrates bone cells & soft tissues.

**2. Ground bone: [Grinding method]**

bone is left to dry, cut into thin transparent slices using a saw & thinner by Carborandum wheel & examined unstained. This method

demonstrates: calcified bone lamellae, lacunae & canaliculi,

Haversian Canals & Volkmann's Canals. [Not used for spongy bone]

**Osteoporosis:** common bone disease e' progressive loss of bone density  $\rightarrow$   $\uparrow\uparrow$  risk of fractures due to  $\uparrow$  bone resorption over bone formation.



**Compact bone** [Ivory bone]

- In shafts of long bones & form outer cover of spongy bone.
- Formed of:

**1. Periosteum:**

- Vascular c.t. w covers bone. Formed of:
    - \* Outer fibrous layer = collagenous bundles + fibroblasts + bl.vs.
    - \* Inner osteogenic (cellular) layer = osteogenic cells w differentiate → Osteoblasts.
- Functions:
1. protection of bone. → thick during growth & fractures.
  2. give nutrition to bone.
  3. " muscle attachment.
  4. growth of bone: osteogenic cells → osteoblasts → form matrix (appositional) → osteocytes.

**2. Endosteum:**

- a single layer of osteogenic cells in a delicate layer of c.t. lining b.m. cavity. functions: protection & growth of bone

**3. Haversian Systems [Osteons]**

= Structural unit of compact bone. = Cylindrical structures parallel to the long axis of bone. Formed of:

- (a) Haversian canal: w contains c.t. rich in bl.vs & nerves, surrounded by
- (b) Concentric bone lamellae: 5-20 concentric layers of calcified osteoid matrix separated by osteocytes inside lacunae & connected by canaliculi through w they get their nutrition.

**4. External Circumferential Lamellae:**

bone lamellae = calcified collagenous bundles separated by osteocytes inside lacunae just under the periosteum & parallel to the bony surface.

**5. Internal Circumferential Lamellae:**

bone lamellae around b.m. cavity & parallel to the endosteum.

**6. Interstitial Lamellae:**

Irregular bone lamellae + osteocytes inside lacunae in bet. Haversian systems.

**\* Volkmann's Canals:**

transverse or oblique canals w connect Haversian canals e' one another to Periosteum & b.m. cavity to get better nutrition.

**\* Perforating fibres of Sharpey:**

= Calcified collagenous bundles that arise from tendons or ligaments & perforate the periosteum to be attached to ext. circumferential lamellae. i.e. they are the continuation of tendons to fix tendons & muscles into the bone.



| Bone Cells                                                                                                                                                                                                                                                                                               |                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                     |  |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|--|
| Osteoprogenitor cell                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                   | bone forming cells                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                     |  |
| Osteogenic Cells                                                                                                                                                                                                                                                                                         | Osteoblasts                                                                                                                                                                                                       | Osteocytes                                                                                                                                                                                                                                                                                                                                 | Osteoclasts                                                                                                                                         |  |
| U.M.Cs & pericytes                                                                                                                                                                                                                                                                                       | - Osteogenic cells                                                                                                                                                                                                | - Osteoblasts                                                                                                                                                                                                                                                                                                                              | fusion of blood monocytes.                                                                                                                          |  |
| Origin                                                                                                                                                                                                                                                                                                   | Inner layer of periosteum & endosteum.                                                                                                                                                                            | imprisoned inside lacunae bet. bone lamellae & connected by canaliculi                                                                                                                                                                                                                                                                     | In cavities called Howship's lacuna on bony surfaces (near p.m. cavity)                                                                             |  |
| L.M.                                                                                                                                                                                                                                                                                                     | <ul style="list-style-type: none"><li>- small flat cell e'</li><li>- flat dark nucleus &amp; pale basophilic cytoplasm.</li></ul>                                                                                 | <ul style="list-style-type: none"><li>- Small branched oval cells</li><li>- N.: central &amp; oval.</li><li>- C.: pale basophilic</li><li>- also contain alk. phosphatase.</li></ul>                                                                                                                                                       | <ul style="list-style-type: none"><li>- large cell e' brush border</li><li>- multinucleated (6-12 nuclei)</li><li>- C: foamy acidophilic.</li></ul> |  |
| E.M.                                                                                                                                                                                                                                                                                                     | <p>Few organelles + features of immature cells i.e. centrioles + free ribosomes.</p> <p>(E.M.) features of ptn. secreting cells i.e. many mit., rich in r.E.R. + well developed G.A. rich in alk. phosphatase</p> | <p>(E.M.) features of active cells but e' less mit., r.E.R. &amp; smaller G.A.</p> <p>The lacunae are connected by canaliculi through w processes are connected by gap junctions for exchange of nutrients &amp; waste products.</p> <p>(N.B.) Osteocytes cannot divide so present singly inside their lacunae No interstitial growth.</p> | <p>(E.M.) has ruffled border = microvilli - rich in mit., G.A., vesicles + lysosomes.</p> <p>(N.B.) Osteoclasts are not phagocyt</p>                |  |
| Bone destruction.                                                                                                                                                                                                                                                                                        |                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                     |  |
| 1. Bone resorbing cells                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                     |  |
| <p>secrete <math>CO_2 + H_2O \rightarrow</math> carbonic acid + <math>H^+</math> <math>\rightarrow</math> acidic medium <math>\rightarrow</math> dissolve Ca <math>\rightarrow</math> decalcification.</p> <p>their proteolytic enzs <math>\rightarrow</math> destroy the organic part of the matrix</p> |                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                     |  |
| 2. Bone remodelling during ossification.                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                     |  |
| 1. Bone Maintaining Cells                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                     |  |
| <p>2. maintain organic part of matrix</p> <p>3. Maintain hardness of matrix by continuous deposition of Ca</p>                                                                                                                                                                                           |                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                     |  |
| 1. Bone forming cells.                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                     |  |
| <p>2. Synthesis of osteoid matrix</p> <p>3. Deposit Ca in the Matrix by alkaline phosphatase</p> <p>4. When completely surrounded by calcified matrix <math>\rightarrow</math> change into Osteocytes.</p>                                                                                               |                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                     |  |
| Functions                                                                                                                                                                                                                                                                                                |                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                     |  |
| <p>1. Give rise to <math>\rightarrow</math> Osteoblasts during growth &amp; healing of fractures.</p> <p>2. In avascular medium <math>\rightarrow</math> may give chondroblasts.</p>                                                                                                                     |                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                                     |  |



# Spongy [Cancellous] Bone

Irregular type of bone 1st formed during fetal life & bone repair.

Sites: • epiphysis of long bone • centre of flat bone . .  
• short bones • irregular bones.

Structure:

Irregular branching & anastomosing bone trabeculae separated by multiple & irregular bone marrow cavities.

Bone trabeculae = irregular bone lamellae & osteocytes.

No Haversian system or Haversian canals.

The bone surface is covered & periosteum & b.m. cavities lined & Endosteum.

## Bone Formation [Ossification]

### 1. Intramembranous Ossification:

In w a membrane of mesenchymal c.t. is changed into spongy bone.  
e.g. in flat bones.

1. 1st Ossific centre appear in the centre of the memb. rich in UMCs + bl.vs.
2. UMCs + pericytes differentiate into osteogenic cells → Osteoblasts  
Osteoblasts secrete osteoid matrix, deposit Ca in the matrix & change into osteocytes.
3. Many ossific centres are formed in the c.t. memb.
4. The irregular bone trabeculae fuse → Spongy bone.
5. UMCs & bl.vs in the spaces bet. bone trabeculae fuse → BM. cells

### 2. Intra-cartilagenous Ossification:

In w a model of cartilage is replaced by mesenchymal c.t. w change into bone e.g. in long bones & irregular bone.

A. 1st Centre of Ossification: [in centre of diaphysis]

- chondrocytes proliferate, enlarge (hypertrophy) & deposit Ca in the matrix  
→ become deprived from nutrition & die leaving empty spaces.
- perichondrium becomes more vascular so, UMCs → osteogenic cells → osteoblasts → thin collar of bone matrix = Subperiosteal collar
- Osteoclasts open holes in the collar to allow bl.vs. + UMCs to invade the cavities.
- UMCs → osteogenic cells w attach to remnants of the calcified basophilic matrix & change into osteoblast. → Form irregular bone trabeculae  
[Spongy bone].
- Osteoclasts resorb central irregular trabeculae → single b.m. cavity  
& UMCs → b.m. cells while osteoblasts deposit new bone [Remodelling]



- Complete Ossification: Osteoblasts form concentric bone lamellae around bl.vs. to form Haversian canals & systems

B]. Secondary Centre of Ossification: in Epiphysis  
Similar to 1<sup>st</sup> centre " " but until spongy bone is formed.

So, cartilage is replaced by bone except in 2 regions:

① Articular cartilage: throughout life      ② Epiphyseal plate: till age of 21-22

Growing End of Bone = [Epiphyseal plate]:

Stages of Intracartilagenous Ossification:

1. Zone of resting cartilage: small scattered chondrocytes.
2. Zone of Proliferation: Chondrocytes  $\uparrow$  in No. & arranged in parallel rows.
3. Zone of Maturation [Hypertrophy]: Chondrocytes  $\uparrow$  in size & accumulate glycogen & alk. phosphatase.
4. Zone of Calcification: Chondrocytes deposit  $Ca^{++}$  in the matrix under the periosteum, so cells die  $\rightarrow$  leaving empty spaces.
5. Stage of Invasion: Vascular bud (bl.vs + UMCs) invade the empty spaces through holes formed by osteoclasts in periosteal collar.
6. Zone of Spongy bone Formation:  
UMCs  $\rightarrow$  osteogenic cells  $\rightarrow$  osteoblasts w/ lay matrix on calcified remnants  $\rightarrow$  bone trabeculae w/ fuse  $\rightarrow$  spongy bone.
7. Remodelling: Osteoclasts resorb central bone trabeculae  $\rightarrow$  central b.m. can.
8. Zone of Complete Ossification: Osteoblasts start to form concentric bone lamellae around bl.vs. to form Haversian canals & Haversian systems.

(N.B.) A stable bl.  $Ca^{++}$  level is reached by balance bet. osteoblasts & osteoclasts. This is hormonally regulated.

Parathyroid hr. stimulate osteoclasts while

Calcitonin " inhibits "

So, Calcitonin is given as a treatment for cases of Osteoporosis.



# Muscles [Striated: skeletal & c. Non-striated: Smooth]

## 1. Skeletal

## 2. Ca

**Site** - attached to skeleton except:  
 • face & tongue • pharynx & upper  $\frac{1}{3}$  of esophagus.  
 • Diaphragm • cremasteric muscle.

- Wall of he  
 • (myocardium)

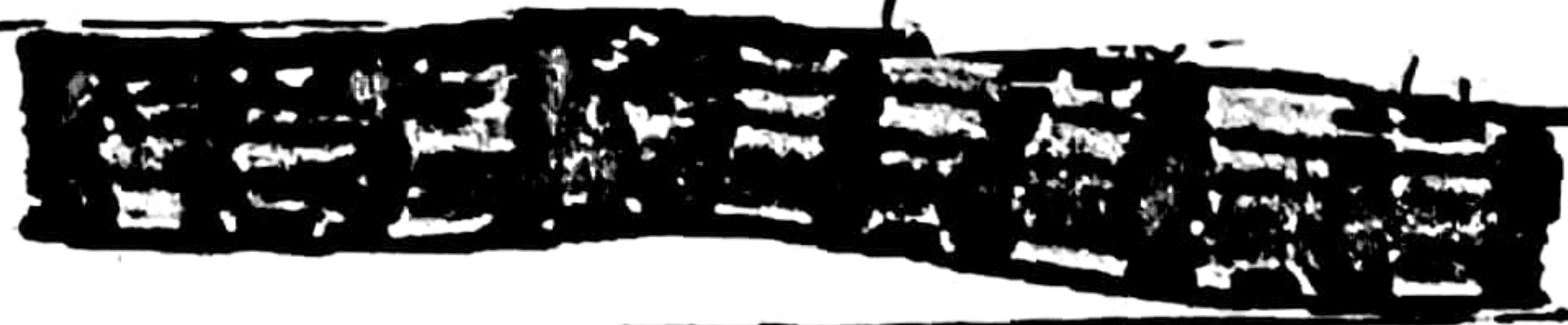
**Action** - Voluntary except " " • pharynx & upper  $\frac{1}{3}$  of oesh.  
 - supplied by motor nerve.

- Involuntary  
 - autonomic: c

**Origin** - mesodermal [fusion of myoblasts  $\rightarrow$  myocytes]  
**Regeneration** - from satellites bet. sarcolemma & basal lamina.

- mesoderm  
 Cannot regenerate

**(L.M.)** length variable  
 size diameter 10 - 100  $\mu$ m.



80  $\mu$ m  
 about 15  $\mu$ m

**Shape** Cylindrical & non-branching except in face & tongue

- Cylindrical, l  
 running in d

**Sarcolemma**: V. thick as it fuses e' basal lamina & endomysium

- this connected by

**Sarcoplasm**: acidophilic

- acidophilic

**Striations**: Clear due to regular myofibrils



- Irregular s

**Nuclei**: Multiple, Oval & peripheral.

- each fibre is  
 each e' single

### (E.M.)

**Organelles**: • Myofibrils: numerous, parallel

شرح

- Fewer my

• mitochondria: numerous, in rows bet. myofibrils  
 (sarcosomes)

- more num

• Sarcoplasmic reticulum: modified S.E.R. around myofibril.  
 Site for  $Ca^{++}$  storage & pump.

- One termin  
 T-tubule (

\* **Triad** • **Tubular system**

\* **Diad**

• few ribosomes, small Golgi around nuclei

- other organelles

**Inclusions**: Myoglobin, glycogen grs., fat droplets bet. myofibrils  
 O<sub>2</sub> binding pig. give energy

- Myoglobin,  
 = waste produ

- Atrial gran  
 • Atrial m

**Intercalated disc** absent

prese

**Type** red, white & intermediate in diff. proportions

red

• **Organization of muscle fibres**:  
 parallel muscle fibres are grouped into bundles covered e' c.t.  
 1. **Epimysium**: dense c.t. that covers the whole muscle  
 2. **Perimysium**: less dense c.t. ~ descend from epimysium & surrounds each bundle.  
 3. **Endomysium**: reticular fs around the fibres.  
 All carry bl. vs. & nerve fibres to nourish the muscle fibres by diff. C.T. connects ms. fs. & is essential for force transmission.



### 3. Smooth

- Wall of bl. vessels.
- Wall of Viscera (respiratory, digestive, urinary) & genital systems
- Skin & eye.

- Involuntary
- autonomic

- Mesodermal [UMC]. On need, can undergo hypertrophy (↑ size) & hyperplasia (↑ No) e.g. in hypertension, pregnancy.
- can regenerate by mitosis or from pericytes in wall of bl. v.
- 20 μm in small vessels  $\rightarrow$  500 μm in pregnant uterus

8 μm.

- Spindle shaped. In L.S. the tapering end is adjacent to the broad part of the adj. cell. In T.S, Have variable diameters.

Thin, covered by basal lamina.

Acidophilic

- No striations as myofibrils are few & overlapping

- Single, central & oval (cigar-shaped)  $\rightarrow$  Cork-screw appearance during contraction.

Sarcolemma: have invaginations (caveola) but No T-tubules so, (No triad)  
the fibres are joined by gap junction.

- Myofibrils: few overlapping: 3 types:
  - $\rightarrow$  thin (actin), thick (myosin) + intermediate (desmin)

- Actin insert into attachment plaques on inner side of sarcolemma & interact with myosin & interact with other actin filaments & insert into intracytoplasmic dense bodies (correspond to Z-line in striated ms)
- desmin filaments also insert into dense bodies
- Mit., SER, ribosomes, G.A. at perinuclear area.

- Myoglobin & glycogen

Absent.

White

Organization of Smooth muscles:

Connected by gap junction, surrounded by endomysium arranged in bundles surrounded by perimysium rich in bl. & r.s.

Functions of smooth muscles:

1. Slow, sustained involuntary contraction modulated by autonomic innervation & hormones.
2. Secrete c.t. fs & matrix e.g. in wall of bl. vs.

Oxytocin = a hormone which stimulates contraction of sm. ms. e.g. essential for uterine contractions during parturition. So used to induce or enhance labor.

strength & rate of contraction

by fibrosis e.g. myocardial infarction.

anastomoses in directions of endomysium

ions + intercalated disc

of cells = myocytes central & oval N.

larger e' mce cristae

double accompany of Z-line

tubular system.

few

gen, fat, lipids in pig

e' age  $\rightarrow$  brown atrophy or heart.

contain diuretic hormones  $\rightarrow$  regulate Na H<sub>2</sub>O balance

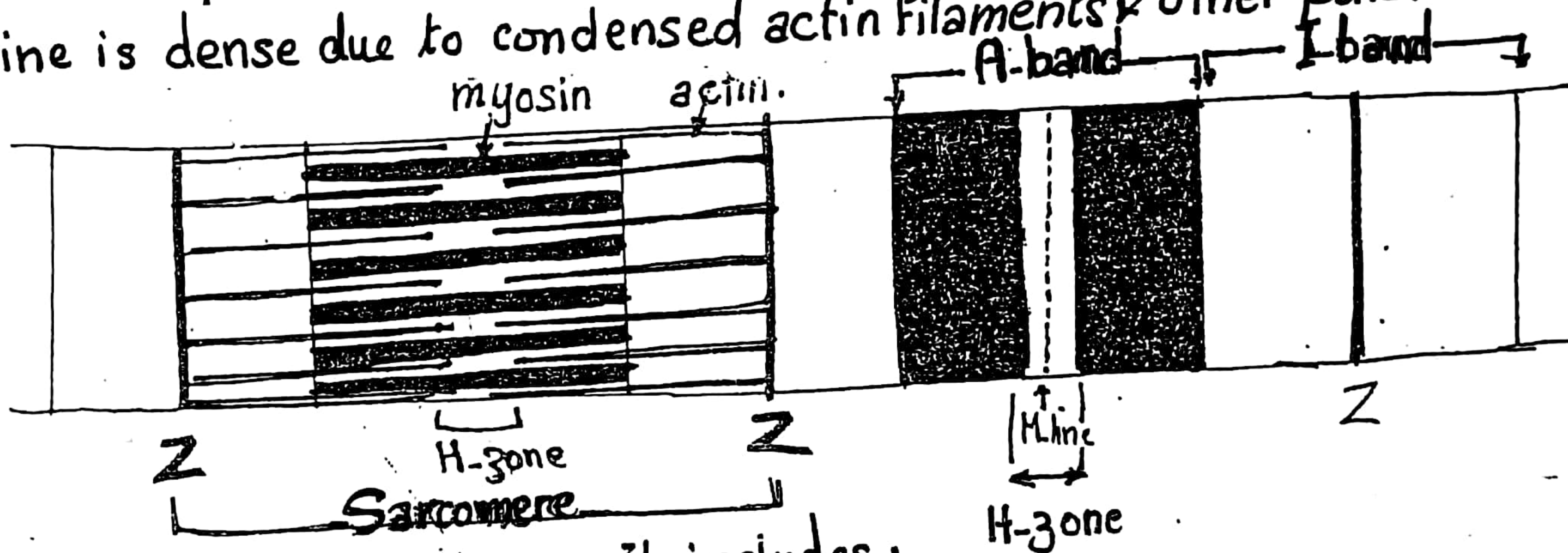
have endocrine function



E.M. of Myofibrils:

- Only I-band is shortened while A band remains constant.

- Z-line is dense due to condensed actin filaments & other ptns.



**Triad of Tubular System** : It includes:

- Triad of Tubular System : It includes:
- a) T-tubule : Formed by invagination of sarcolemma into the sarcoplasm.

- Its cavity is continuous with the sarcoplasm like a collar at the vertex of the myofibril
- It extends transversely into the sarcoplasm

- 2 Sarcoplasmic tubules:**  
- modified parts of sarcoplasmic reticulum & continuous w/ it. It forms t.v. terminal cisternae. Each 2 tubules surround one t.v. T-tubule forming Triad

The Role of Tubular System in muscle contraction: Function of SK

As the nerve impulse reaches the T-tubule to sarcoplasmic reticulum w  
Depolarization spreads along the T-tubule to sarcoplasmic reticulum w  
pump  $Ca^{++}$  → gliding of actin over myosin till the middle of the A-band

**During Contraction:**

- During Contraction:  
 I band become shorter, H-zone disappears while A-band remains constant.  
 muscle fibres become shorter (length change)

- I band become shorter, H zone disappear
- Sarcomeres & muscle fibres become shorter
- the length of actin & myosin filaments do not change
- Relaxation stops:  $Ca^{++}$  is actively transported to the

- Sarcomeres & muscle fibers
- The length of actin & myosin filaments do not change
- After depolarization stops:  $\text{Ca}^{++}$  is actively transported to the SER  $\rightarrow$  muscle relaxation



## Types of skeletal muscle fibres:

Formed of 3 types of fibres in diff. proportions: red, white & intermediate. (4)

| I Red                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | II White                                                                                                                                                                                                                                                                                                                                                                                       |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"><li>• red color due to: 1, 2, 3</li><li>1. rich in myoglobin (aerobic) <sup>respiration</sup></li><li>2. More numerous &amp; larger mitoch.</li><li>3. rich vascularity</li><li>• smaller diameter</li><li>• less glycogen</li><li>• more sarcoplasm</li><li>• fewer myofibrils</li><li>• Irregular striations</li><li>• F. slow sustained (prolonged) contractions without fatigue</li><li>• Examples: - athletic ms. [marathon runners]</li><li>- long muscles of back [in humans] (erect posture)</li><li>- Chest ms of birds</li></ul> | <ul style="list-style-type: none"><li>- white due to:</li><li>1. poor (anaerobic by glycolysis)</li><li>2. less</li><li>3. poor</li><li>- larger</li><li>- more glycogen</li><li>- less</li><li>- full of myofibrils</li><li>- regular striations.</li><li>- Fast, short contractions &amp; easy fatigue.</li><li>- muscles of eye &amp; digit</li><li>- short distance sprinter ms.</li></ul> |

III - Intermediate fibres & intermediate characters bet. red & white fib.

The types of fibres have a clinical significance in muscle biopsy to diagnose muscle diseases due to mitochondrial disorders.

## Musculo-tendinous Junction:

Muscle fibres stop & the c.t. components of the ms. continue & the tendon.

## General Characteristics of muscular tissue:

1. Mesodermal.: UMC  $\rightarrow$  myoblasts  $\rightarrow$  myocytes (in all types of ms)
2. the structural & functional unit = Muscle fibre.
3. the cell memb. of muscle fibre = Sarcolemma.
4. " cytoplasm " " = Sarcoplasm.
5. Sarcoplasm: acidophilic & contains:  
all organelles: (mit., sER & myofibrils) &  
inclusions (myoglobin, fat & glycogen).
6. s-ER is called sarcoplasmic reticulum.

**Muscle dystrophy:** progressive degeneration of skeletal ms. fs & Satellite cells fail to replace them  $\rightarrow$   $\downarrow$  muscle function.



## Intercalated discs:

\* def.: the cell memb. of adjacent cardiac myocytes that form the cardiac ms. fs.

L.M.: dense lines at intervals along the length of the cardiac ms. fibres.

E.M. Have the shape of stairway & 2 regions (l.v. & lat.) & 3 types of Junction

1. l.v. component: at right angle to the fibre [riser of stairway] contains Desmosomes & adherens J. (fascia adherens): prevent their separation during contraction.

2. lat. component: parallel to the fibre [step of stairway]: have gap J: allows impulses to pass from one cell to the other. Their site protects them from contraction forces.

## Function of Cardiac muscle:

Involuntary, spontaneous rhythmic contraction controlled (but not initiated) by autonomic innervation & hormones.

The wall of heart: 2 atria & 2 ventricles. Formed of 3 layers:

1. Epicardium = visceral layer of pericardium.

2. Myocardium = cardiac muscle fibres: thicker in ventricles than in atria.

3. endocardium = the lining endothelium from inside.

## Valves of Heart:

= Folds of endocardium = middle layer of dense fibrous c.t. rich in collagenous & elastic fibres + macrophages covered e' s. squamous endothelium.

## Purkinje Muscle Fibres

- modified Cardiac ms. fs. present in the A.V bundle & its branches.

- Conduct impulses faster than cardiac ms. fs. grouped into bundles surrounded by c.t. sheath.

## Histological characters of Purkinje fibres:

1. Larger in diameter than cardiac muscle.

2. Have paler sarcoplasm as it is rich in <sup>\*</sup>glycogen (dissolves during preparation) so appears vacuolated. <sup>\*</sup>mitochondria.

3. have <sup>\*</sup>few myofibrils w are peripherally situated.

4. No striations.

5. No intercalated discs.

6. have one or 2 eccentric nuclei.



-2-

\* In Myocardial infarction:  
 Cardiac ms. release cardiac enzs as troponin T + creatine Kinas  
 So, any patient presenting c' chest pain is advised to  
 measure these enzs in the bl. for early diagnosis & tx.

### Differences bet. the 3 types of muscles.

|                         | Skeletal                | Cardiac                                                                                                                                             | Smooth                       |
|-------------------------|-------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------|
| Site                    | - Attached to skeleton  | - Wall of heart                                                                                                                                     | - Wall of Viscera.           |
| Size                    | - Largest               | - Med. sized                                                                                                                                        | - smallest                   |
| Shape                   | - Cylindrical &         | - Cylindrical &                                                                                                                                     | - spindle-shaped.            |
| branching               | - rarely branch         | - branched                                                                                                                                          | - non-branched.              |
| Sarcolemma              | - Thick                 | - V. thin                                                                                                                                           | - thin.                      |
| Striations              | - Striated              | - Nonclear striations                                                                                                                               | - Non-striated.              |
| Sarcomere               | - regular               | - Irregular striations.                                                                                                                             | - absent.                    |
| Tubular system          | - Triad                 | - Diad                                                                                                                                              | - absent.                    |
| type                    | - red & white           | - red                                                                                                                                               | - white.                     |
| Nuclei                  | - Multiple & peripheral | - single & central                                                                                                                                  | - single, central            |
| Cell Junct <sup>n</sup> | - absent                | 3 types $\left\{ \begin{array}{l} \rightarrow \text{F. adherens} \\ \rightarrow \text{Desmosomes} \\ \rightarrow \text{gap J.} \end{array} \right.$ | - gap junction.              |
| Action                  | - Voluntary (motor)     | - Involuntary (autonomic)                                                                                                                           | - Involuntary (autonomic)    |
| Regenerat <sup>n</sup>  | - From satellites.      | - cannot regenerate                                                                                                                                 | - mitosis or from pericytes. |
| Single fibre            | - Single cell.          | - many cells.                                                                                                                                       | - single cell.               |
| Modificat <sup>n</sup>  | - Muscle spindle        | - Purkinje fs.                                                                                                                                      | —                            |



# Nervous Tissue

Have 2 types of cells: Neurons + glial cells

## Neurons

The structural & functional unit of nervous tissue. Formed of:  
Cell body [perikaryon] & its processes [axon & dendrites].

### Classification of neurons:

#### A. According to No. of processes: [polarity]:

(1) **Unipolar**: Have a single process that divides into 2 branches (T-shaped) one extends to a peripheral endings & acts as a dendrite but structurally it is similar to axon. & the other towards CNS & act as an axon. The impulse travels from the dendrite to the axon directly without passing through the perikaryon e.g. in spinal ganglia & mesencephalic nucleus of trigeminal nerve.



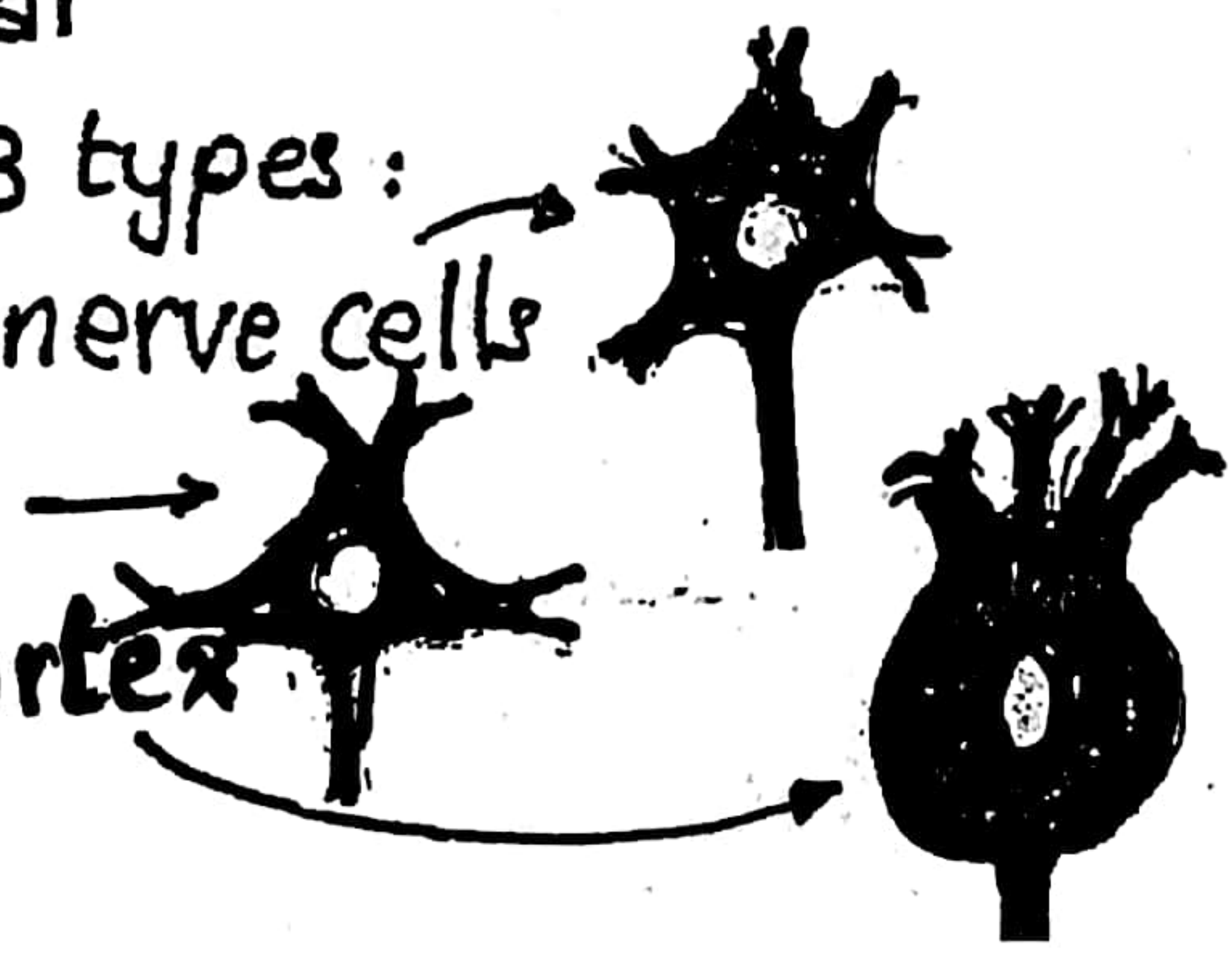
(2) **Bipolar**: have one dendrite & one axon e.g. in retina of eye, olfactory mucosa, cochlear & vestibular ganglia of ear

(3) **Multipolar**: have one axon & many dendrites: 3 types:

Stellate: e.g. AHCs in sp. cord & sympathetic nerve cells

Pyramidal: e.g.  $\Delta$  cells in cerebral cortex.

Pyriform: e.g. Purkinje cells in cerebellar cortex



#### B. According to function:

(1) **Sensory neurons**: receive sensory stimuli e.g. post. root ganglia.

(2) **Motor neurons**: control effectors as muscles & glands e.g. AHCs.

(3) **Interneurons**: connect neurons as in retina & sp. cord.

#### C. According to length of axon:

(1) **Golgi type 1**: have long axon that leaves the grey matter & enters the white matter e.g. motor neurons in the sp. cord,  $\Delta$  cells in cerebral cortex, Purkinje cells in the cerebellar cortex.

(2) **Golgi type 2**: have short axon that does not leave the grey matter & never enters the white matter e.g. interneurons in cerebral & cerebellar cortex.



# Structure of Neurons :

## Cell body [Perikaryon]:

= The part of the neuron containing the nucleus & surrounding cytoplasm.

**Size** : varies from  $4\mu\text{m}$  as in granular cells of cerebellum to  $100\mu\text{m}$  as in AHCs.

**Shape** : unipolar (globular), bipolar (fusiform), Multipolar { stellate.  
pyramidal.  
pyriform.

**Nucleus** : large, rounded, euchromatic & prominent nucleolus.

**Cytoplasm** : contains :

1. **mitochondria** : scattered throughout the cytoplasm.

2. **Golgi apparatus** : around the nucleus. stained e' Ag.

3. **Neurofilaments** : intermediate filaments (10 nm) in the perikaryon & processes to provide structural support. Fixatives gather them into bundles ( $2\mu\text{m}$ ) called neurofibrils (visible by L.M. & stain brown e' Ag)

4. **Microtubules** : (25 nm) arranged in bundles in the perikaryon & processes for transport of neurotransmitter along the axon.

5. **Centrioles** are absent, so neurons cannot divide.

6. **Nissl bodies** : basophilic granules = segments of rER & numerous polyribosomes to form both structural proteins & protein for transport

The N<sup>o</sup> varies according to the type & function of the neuron. present in nerve cell & dendrites, absent in axon & axon hillock.

7. **Inclusions** :

a. lipofuscin (golden brown) - undigested material in lysosomes, ↑↑ e' age.

b. melanin (brown or black) in Substantia nigra of midbrain

c. fat droplets (energy reserve)

| Processes: Dendrites                                                                                                                                                                                                                                                                                                                       | Axon                                                                                                                                                                                                                                                                                  |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>Multiple, short &amp; thick.</li> <li>Branch like a tree (branches arise at acute angle.</li> <li>become thinner towards its end.</li> <li>Have Nissl granules.</li> <li>Covered e' processes (dendritic spines) for synaptic contact.</li> <li>Carry nerve impulses towards the n. cell</li> </ul> | <ul style="list-style-type: none"> <li>Single, long, thin.</li> <li>Do not branch except at its end</li> <li>may give collateral (at right angle)</li> <li>Have uniform diameter.</li> <li>No Nissl granules</li> <li>No spines.</li> <li>carry impulses away from n. cell</li> </ul> |
| Both have mitochondria, neurofibrils & neurotubules.                                                                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                       |



## Synapse

• def.: the site of contact bet. neurons or bet. neuron & effector ↳ muscle  
↳ gland

### Histological Structure:

#### 1. Presynaptic side: (axon terminal)

rich in mit. + synaptic vesicles (contain chemical transmitter) in chemical synapse. It shows separate zones of dense cytoplasm.

#### 2. Synaptic cleft: 20-30 nm: shows delicate fibres.

#### 3. Postsynaptic side:

Has receptors for the chemical transmitter. Have continuous zone of dense cytoplasm associated w' network of filaments = synaptic web.

### • Classification:

#### A. According to way of transmission of n. impulse:

(1) Chemical: (most common) in w' electric impulse from presynaptic memb. is converted into chemical signal to act on postsynaptic side.

(2) Electrical: in w' ionic signal pass through gap junction bet. pre & post. synaptic membranes.

#### B. According to site of contact of the axon:

(1) Axosomatic: axon synapse w' cell body.

(2) Axodendritic: " " " " dendrite

(3) Axoxonic: " " " " axon

#### C. According to relative thickness of cytoplasmic densities on pre & post synaptic membranes:

##### (1) Asymmetric

- the postsynaptic density is thicker
- the synaptic cleft is about 30 nm

##### (2) Symmetric

- the pre & post synaptic densities are similar
- synaptic cleft: about 20 nm



## (Nerve fibre):

Axon, covered by axolemma & contains cytoplasm = axoplasm

The conical expansion at its origin from the nerve cell = axon hillock

## Types of nerve fibres:

### 1. Unmyelinated : (no myelin sheath):

↳ Unmyelinated & out neurolemma [naked] e.g. in grey matter.

↳ Unmyelinated & neurolemma e.g. in post ganglionic sympathetic fibre

### 2. Myelinated : (have myelin sheath):

↳ myelinated & out neurolemma e.g. in white matter.

↳ myelinated & neurolemma e.g. in peripheral nerves.

## Neurolemma [Schwann Cells]

Flat cells & flat nuclei around the myelin sheath.

### Functions:

1. Insulation of nerve impulse.

2. Formation of myelin sheath in peripheral nerves.

3. Regeneration of n. fibres where the axon runs along the path formed by Schwann cells.

## Myelin Sheath

- A lipoprotein sheath, so dissolves during preparation, but stains black & osmic A.

- It is interrupted at intervals [Nodes of Ranvier] = the spaces bet. adjacent Schwann cells.

- The nodes divide m. sheath into segments called internodal segments.

- Formed by rotation of Schwann cells (in PNS) or oligodendrocyte several times around the axon. (CNS)

- By E/M. = fused spiral laminae of cell memb.

## Stages of Myelination:

1. axon invaginates into Schwann cell (in PNS) or oligodendrocyte (CNS) & become surrounded by single turn of cell memb.

2. The cell rotates several times (up to 50) in a spiral form around the axon & the cytoplasm is squeezed → compaction of the turns

3. the fused cell memb. of the turns → myelin sheath.

### In PNS

Schwann cell wraps around 1 segment of 1 axon.

- Function: ↑↑ speed of nerve impulse.

### In CNS

Oligodendrocytes wrap around one segment of many axons (10-60)



# Peripheral Nervous System

Nerves

ganglia

n. endings

## Nerve Trunk

The Nerve is covered e' dense c.t. = Epineureum.

• Nerve fibres are arranged in bundles surrounded by Perineureum.

= Flat epith. like cells joined by tight junction = Barrier to protect n. fibres.

• Nerve fibres are connected by Endoneureum [Sheath of Henle] = reticular fibres formed by neurolemma.

• In H & E sections, myelin dissolves. Can be stained e' Osmic A → black rings.

## Ganglia

def.: Collection of nerve cells outside the CNS. covered e' c.t. capsule.

2 types

→ Spinal (sensory)

→ autonomic (sympathetic & parasympathetic).

| Spinal ganglion                                                                             | Sympathetic                                                                |
|---------------------------------------------------------------------------------------------|----------------------------------------------------------------------------|
| 1. Covered e' thick c.t. capsule                                                            | - thin c.t. capsule                                                        |
| 2. Cells → unipolar<br>→ Variable in size<br>→ larger cells<br>→ arranged in groups or rows | - multipolar stellate.<br>- uniform in size.<br>- smaller.<br>- scattered. |
| 3. Cells are surrounded by large No. of satellite cells.                                    | - few satellites.                                                          |
| 4. Have <b>Glomerulus</b> = coiling of the axon at its beginning from the n. cell.          | - No glomerulus.                                                           |
| 5. Nerve fibres : myelinated                                                                | - Non-myelinated n. fibres.                                                |
| 6. Less bl. vessels.                                                                        | - more bl. vs.                                                             |
| 7. No synapse bet. cells.                                                                   | - present.                                                                 |

Function: relay station for n. impulses.



## Degeneration & Regeneration of Nerves

On nerve injury, there are 2 types of changes:

### 1. Retrograde degeneration:

Changes in the nerve cell & proximal part of nerve fibre:

1. The nerve cell [Perikaryon]: swell, loses dendrites & become globular
2. The nucleus: becomes eccentric
3. Chromatolysis: Nissl bodies disappear → less basophilia.
4. Mitochondria & G.A.: disappear.
5. Neurofibrils: fragment & disappear
6. Lysosomes: ↑↑.

### 2. Wallerian degeneration:

Changes in the distal part of the nerve fibre:

- The axon: (neurofibrils) become beaded, segmented & finally disappear
- Myelin sheath: the internodal segments [fermentation chambers] as fat splits into F.A.s & widening of Nodes of Ranvier.
- Schwann Cells: proliferate → Column of cells to guide axons during regeneration

### Stains for site of degeneration:

1. Ag.: for changes in G.A. & neurofibrils.
2. Basic stain: changes in Nissl gr.
2. Osmic A.: " " " myelin sheath.
3. Weigert-Pal stain: for normal myelin sheath.
4. Marchi stain: Potassium dichromate is used to oxidize the normal myelin then osmic A is used to stain the degenerated myelin & not oxidized tracts.

### Regeneration:

**Macrophages**: remove debris & secrete **interleukin 1 $\alpha$**  stimulates Schwann cells to secrete **substances** that **promote nerve** growth.

Axons grow in direction of the columns of Schwann cells

Regeneration is efficient when there is **no infection**, **intact neurolemma** when n. fibres & schwann cell columns are directed to the correct place

\* When there is a gap bet. the distal & proximal ends of the axon or no distal segment (amputation of a limb), the new n. fibres may form a swelling [neuroma] & spontaneous pain.



# Neuroglia

def.: They are the supportive, nutritive & protective tissue bet. neurons.  
(10 times more than neurons). Types:

## 1. Macroglia: [astrocytes]:

- large star shaped cells e' many processes.
- ectodermal in origin.
- Have large pale nucleus
- E.M. have bundles of intermediate filaments to keep their shape
- Have centrioles (can divide)

| 2 Types: | Cytoplasmic Astrocytes                                                                                                                               | Fibrous astrocytes                                                                                                                                             |
|----------|------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
|          | <ul style="list-style-type: none"> <li>- In grey matter</li> <li>- many short &amp; thick processes</li> <li>- cytoplasm rich in granules</li> </ul> | <ul style="list-style-type: none"> <li>- In white matter.</li> <li>- fewer thin &amp; long processes</li> <li>- less granular &amp; more fibrillary</li> </ul> |

- Functions:
1. Structural support.
  2. Their processes end by expanded end feet on bl. vessels to get nutrition. (metabolic exchange e' blood)
  3. Blood brain barrier.
  4. Repair by forming scar tissue.

## 2. Microglia [Mesoglia] = [Brain Macrophages]

- Small spindle-shaped cells e' many processes.
- The cell & processes are decorated by spines.
- Mesodermal in origin
- Have oval dark nucleus & little cytoplasm.
- Phagocytic cells - In grey & white matter.
- Stained e' vital stain e.g. trypan blue.
- No centrioles.

## 3. Oligodendrocytes:

- Small branched cell e' few processes.
- Ectodermal in origin
- Have small dark nucleus & cytoplasm rich in mit. G.A, ER, ribosome.
- Present in both grey & white matter
- Have centrioles.

| 2 types:  | Satellite Oligodendrocytes    | Interfascicular Oligodendrocytes          |
|-----------|-------------------------------|-------------------------------------------|
| site:     | In grey matter                | In white matter                           |
|           | around nerve cells of neurons | In bet. bundles of axons.                 |
| Function: | support nerve cells           | Form myelin sheath, insulate n. impulses. |



## 4] Ependymal Cells:

- Simple cuboidal or columnar ciliated epith. - Ectodermal in origin.
- lining the central canal of sp. cord & brain ventricles.
- Cilia propel the CSF.

## 5] Schwann cells:

- Around peripheral nerves.
- Ectodermal in origin.
- Functions:
  - insulation of nerve impulses
  - formation of myelin sheath.
  - regeneration of nerves

## 6] Satellite Cells:

- Cubical cells around nerve cells of ganglia. F. supportive.

## Functions of Neuroglia:

| Cell type           | Function                                                                                |
|---------------------|-----------------------------------------------------------------------------------------|
| 1. Astrocytes       | 1. metabolic exchange (nutrition).<br>2. support<br>3. bl. brain barrier.<br>4. Repair. |
| 2. Microglia        | phagocytosis.                                                                           |
| 3. Oligodendrocytes | Insulation & myelin production (in CNS)                                                 |
| 4. Ependymal cells  | lining cavities of CNS → CSF.                                                           |
| 5. Schwann cells    | Insulation, myelin production & regeneration (in PNS)                                   |
| 6. Satellite cells  | support nerve cells in ganglia.                                                         |

\* demyelinating disease: damage of myelin sheath of n. fibres to transmit.

\* Brain tumors: adult ne but glial cells & Schwann

\* Neural stem cells: are in stimulation can replace accidents or diseases.



# Nerve Endings

## A. Receptors

receive stimuli int. or ext. & send impulses

Classified into:

- Exteroceptors: receive ext. stimuli
- Proprioceptors: " stimuli from ms.
- Interoceptors: " int. stimuli.

## Nerve endings in Epithelium

### A Receptors [Exteroceptors]:

#### 1. Free nerve endings:

- naked nerve fibres penetrate the b.m. & enter bet epith. cells.
- Site: in epidermis of skin & cornea.
- Function: receptor for pain (nociceptor), temp. (thermoreceptor), touch, pressure & itching.

#### 2. Merkel's disc:

- naked n. fs end in disc like expansion under Merkel cells bet. basal cells of epidermis
- Site: epidermis of thick skin (palms & soles).
- Function: mechanoreceptor (touch & press).

#### 3. Peritrichial n. endings:

- naked nerve fs around hair follicles
- Function: mechanoreceptor (touch & hair movement)

#### 4. Neuroepithelial Ending:

- taste buds in tongue (taste)
- Organ of Corti in ear (hearing)
- Crista ampularis, macula utriculi, macula sacculi in ear (equilibrium)

## B. Effectors

Conduct impulses to effectors  
[muscles or glands]



### B Effectors:

unmyelinated n. fs form a network around acini of glands as salivary & lacrimal gls. then, branches penetrate the b.m. & end bet the bases of the cells. F: autonomic regulation of secretion.



# Nerve endings in C.T.

All are receptors

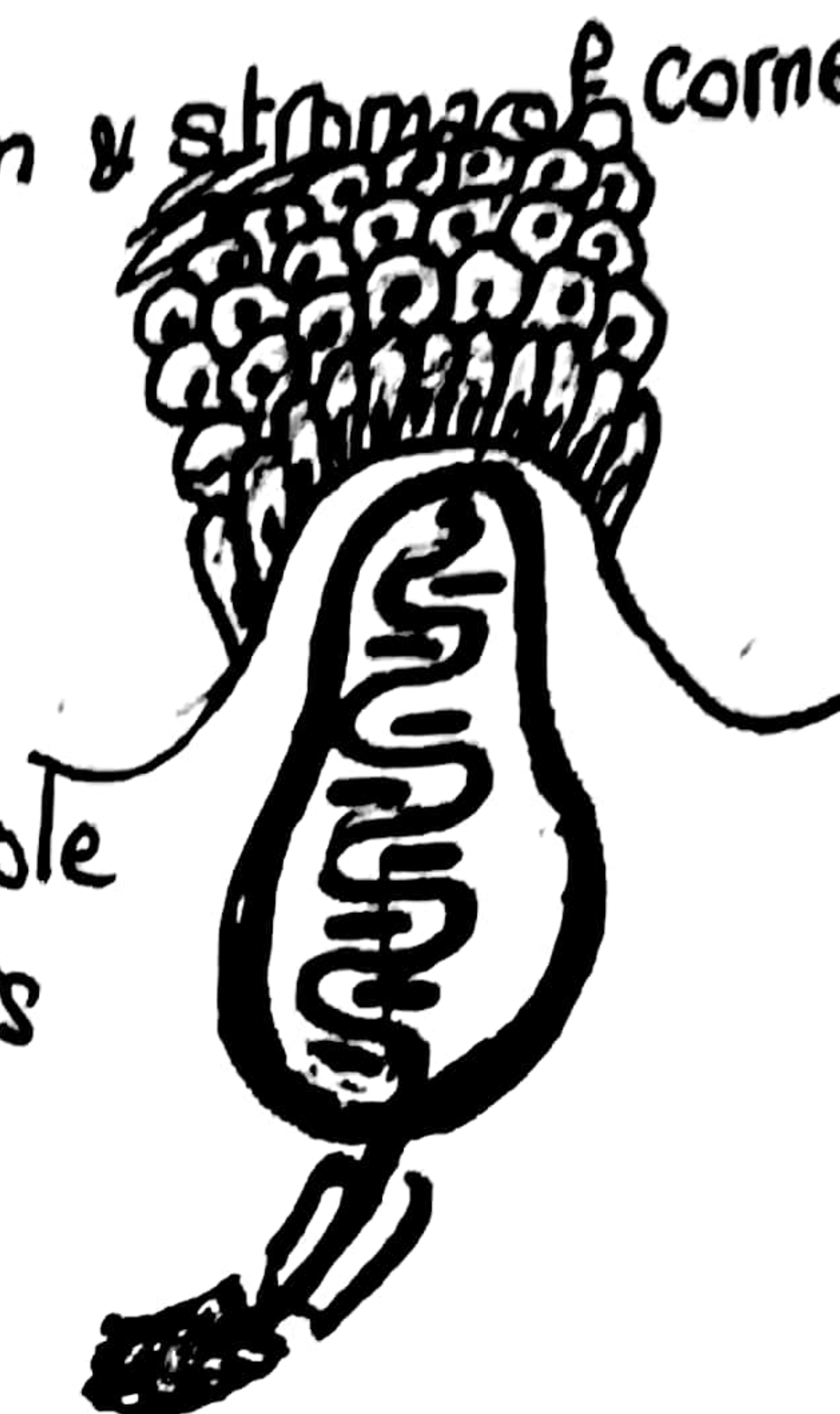
- 2 -

## 1. Free n. endings:

- similar to those in epith. - site: dermis of skin & stroma of cornea.

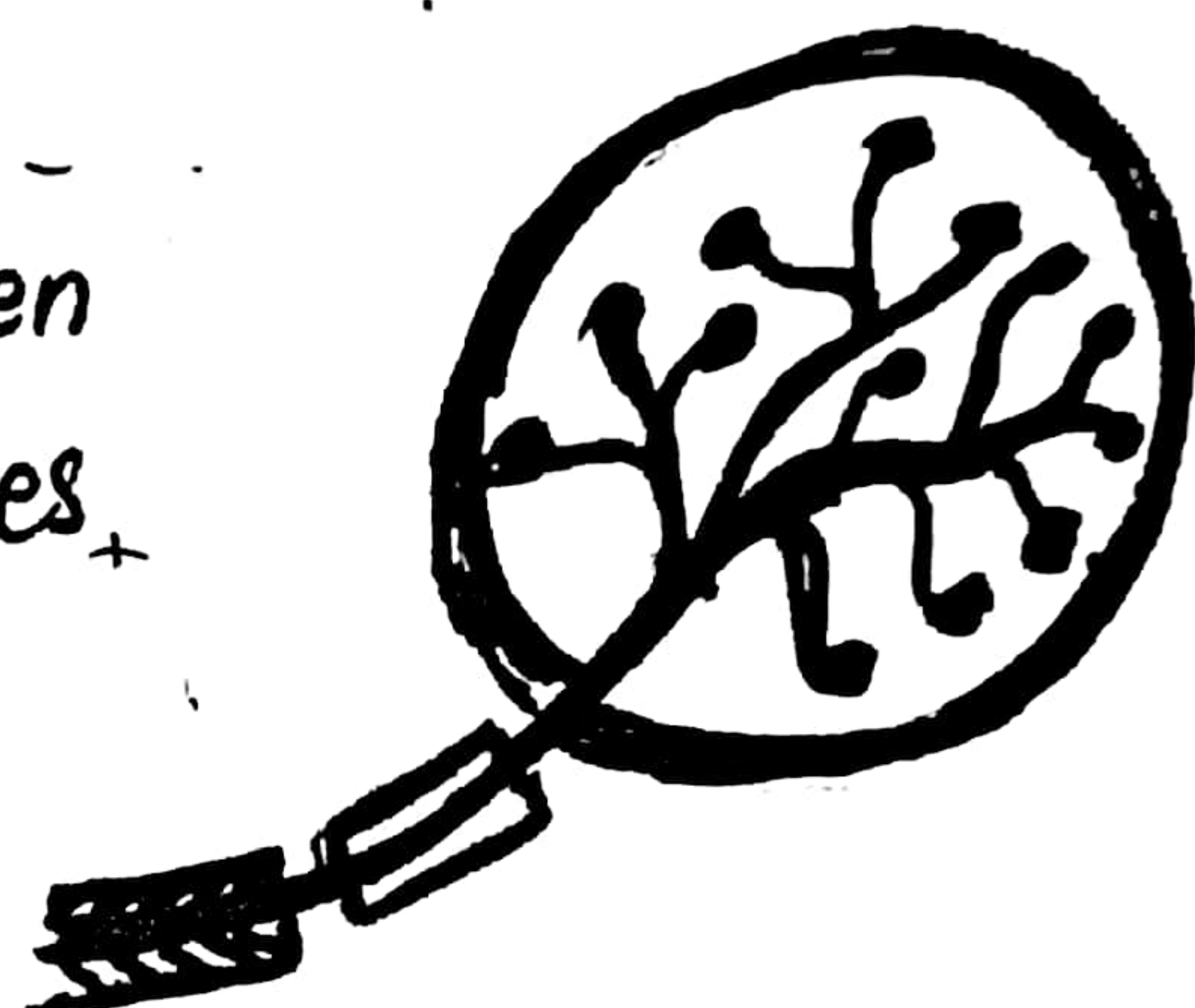
## 2. Meissner's Corpuscles:

- pear shaped. - covered e' c.t. capsule
- the axon loses the myelin sheath & neurolemma & spirals up bet. cell layer to end at the upper pole
- Site: dermal papillae of skin esp. tips of fingers
- Function: mechanoreceptor (touch)



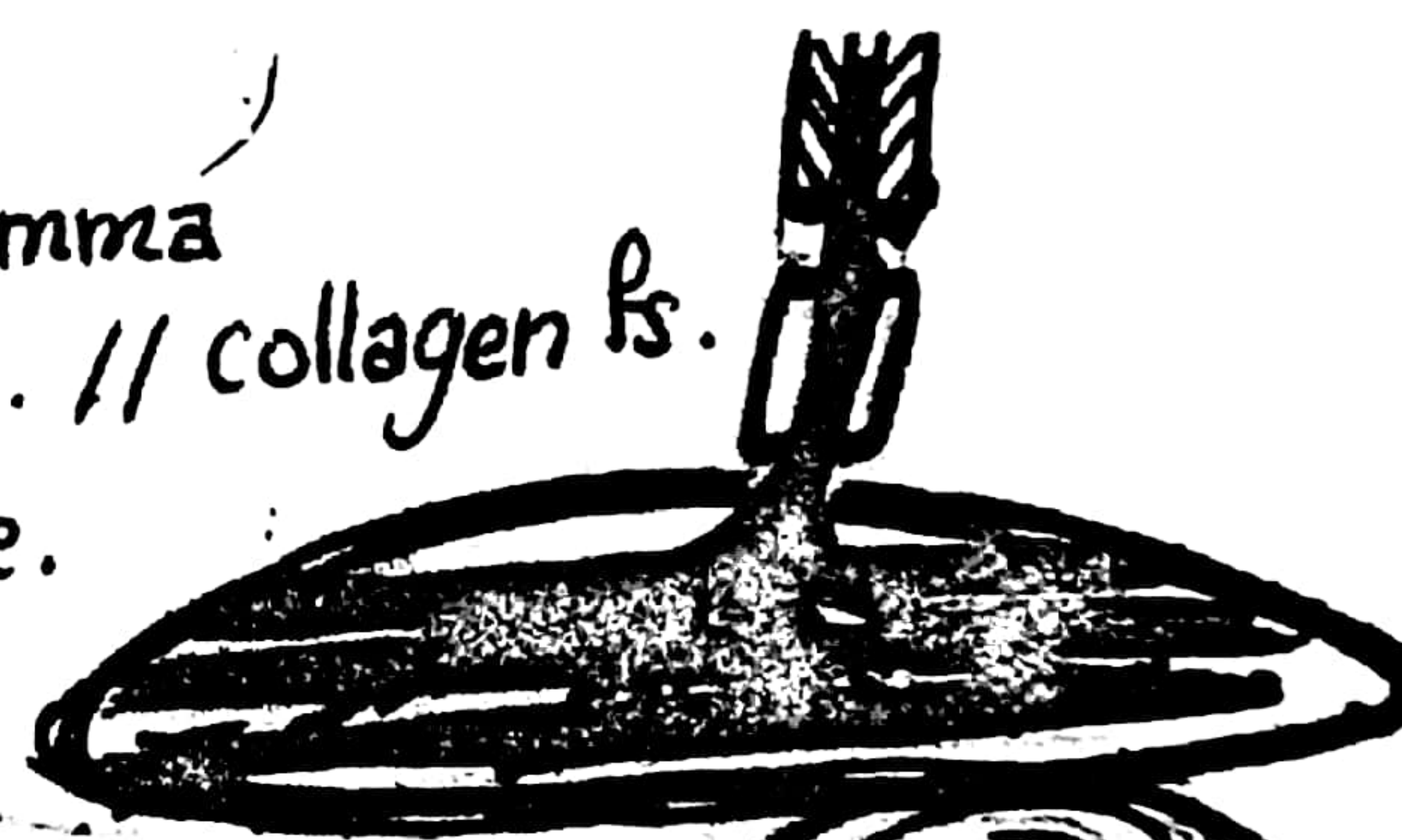
## 3. Krause's end bulb:

- spherical shaped - covered e' c.t. capsule
- the axon loses the myelin & neurolemma then penetrate the capsule & give many branches
- Site: deep in dermis of skin.
- Function: mechanoreceptor (touch)



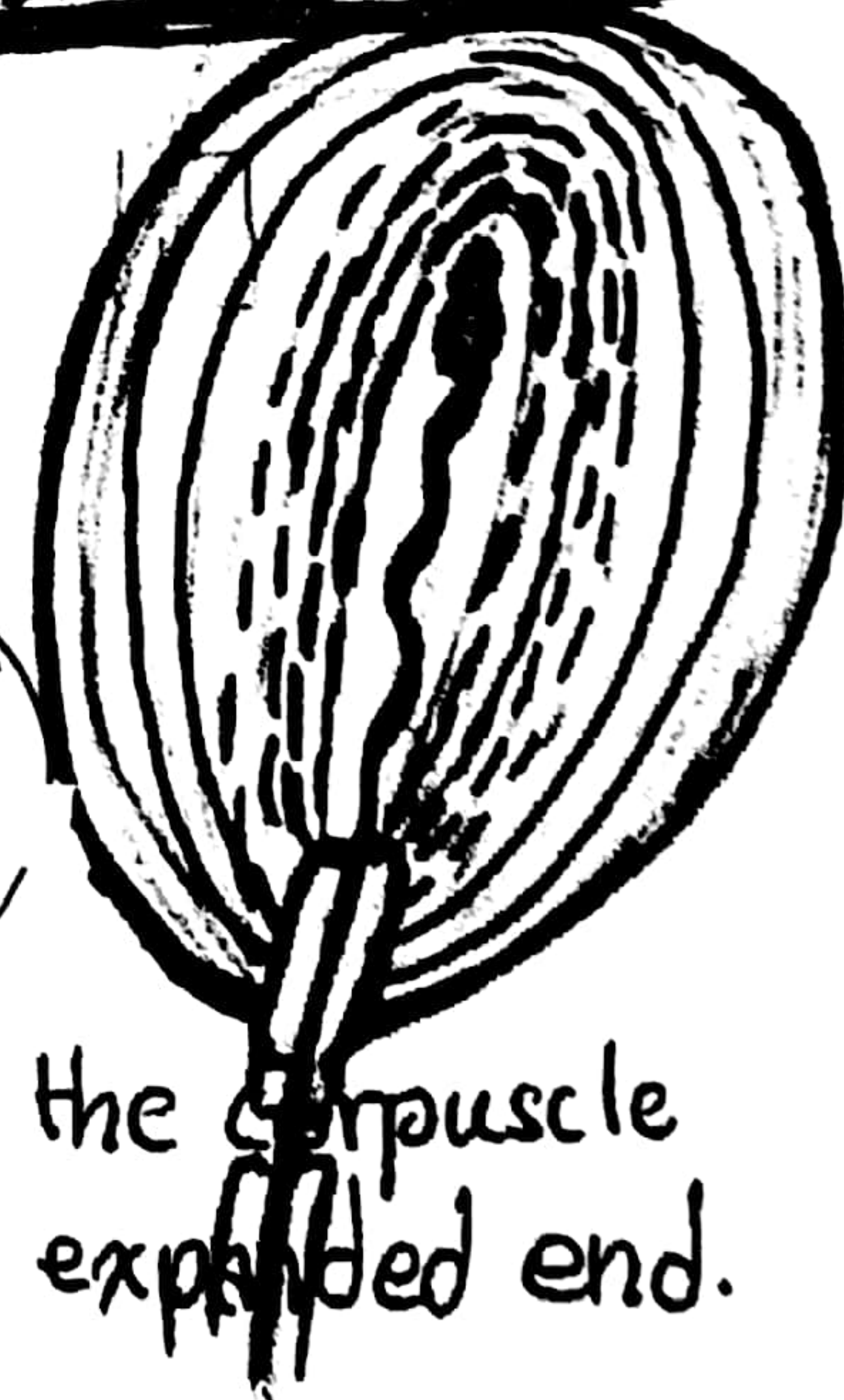
## 4. Ruffini Organ:

- fusiform. - covered e' c.t. capsule
- the axon loses the myelin sheath & neurolemma then penetrate the capsule & branches bet. // collagen fs.
- Site: deep in dermis of skin esp. sole.
- Function: mechanoreceptor (touch).



## 5. Paccinian Corpuscle:

- Oval (1mm long). - covered e' c.t. capsule
- enclose 20-60 concentric lamellae of flat cells (modified schwann cells) closely packed towards t. the centre. e' gel like material bet. them.
- the neurolemma of the axon becomes continuous e' the capsule. It loses the myelin sheath inside the corpuscle
- the naked nerve runs along the long axis & end in expanded end.
- Sites:
  - dermis & hypodermis of **skin**.
  - periosteum of **bone**.
  - capsule of **joints**
  - c.t. of some organs e.g. **pancreas**.

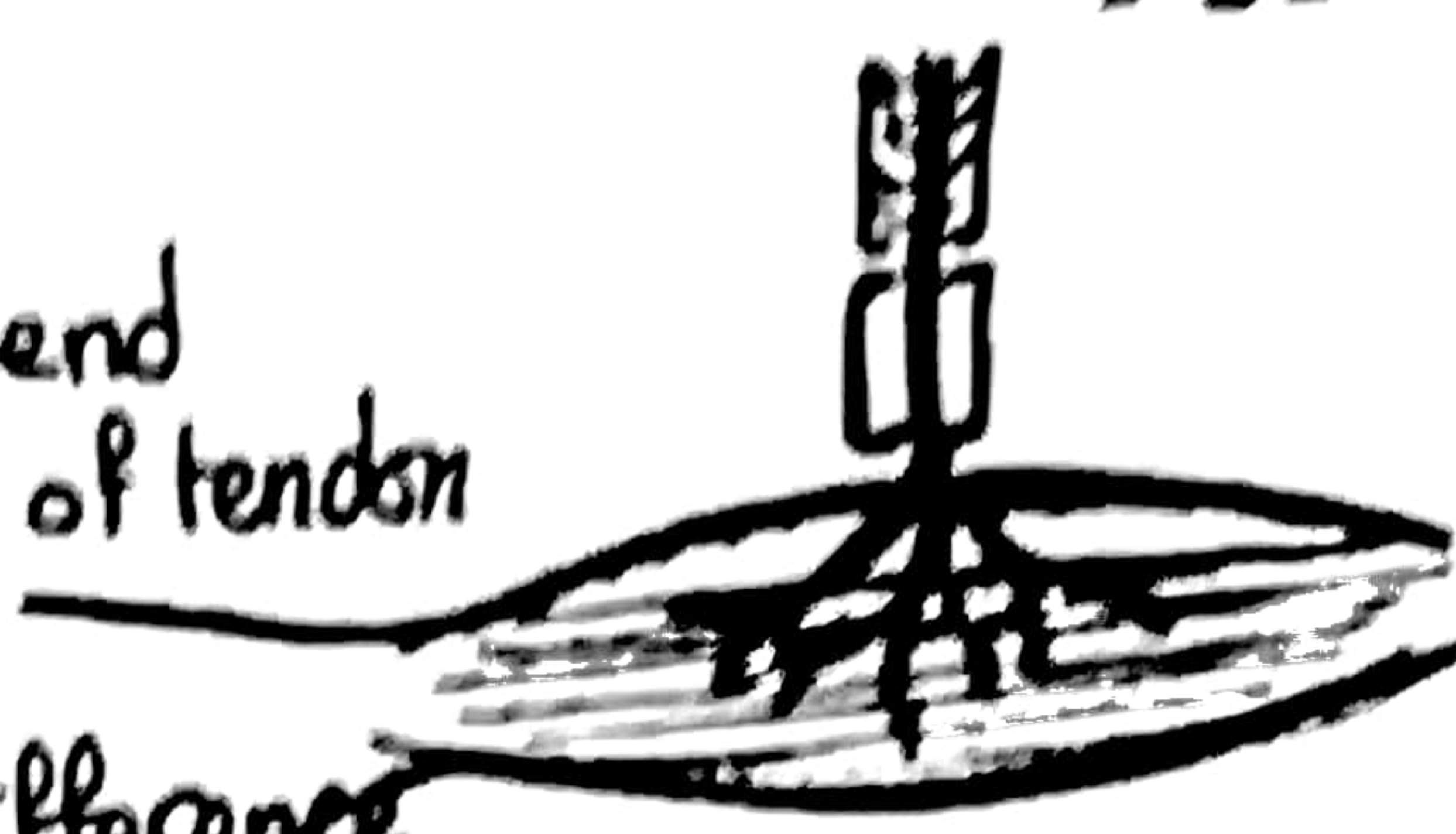


Functions: **Proprioceptor**: mechanoreceptor for pressure, vibration & tension



## 6. Tendon Spindle (Golgi tendon Organ):

- spindle shaped
- covered e' c.t. capsule.
- the naked nerve fs penetrate the capsule to end around collagen bundles continuous e' those of tendon
- Site: tendon near the muscle insertion.
- Function: proprioceptor: conduct data (difference in tension among tendons) to CNS to coordinate muscle contraction



## Nerve Endings in Muscular tissue

Receptors: proprioceptors:

### Muscle Spindle:

- fusiform in shape (6mm long & 1mm in diameter)
- Covered e' thin c.t. capsule.
- the subcapsular space contains:
  - tissue fluid, (lymph)
  - intrafusal ms fibres
  - n. fibers.
- the intrafusal muscle fs. are smaller than skeletal ms e' central non striated part containing nuclei: there are 2 types:
  - a. nuclear bag type: have central dilated nuclear area
  - b. " " chain " : not dilated & have a chain of central nuclei
- Innervation:

- \* Afferent Innervation:
- i. Annulospiral ending: large unmyelinated n. fs w end spirally around the non-striated central parts of the intrafusal ms. fs.
- ii. Flower spray ending: small unmyelinated n. fs w end on the peripheral striated parts of the intrafusal ms fs.

### \* Efferent Innervation:

gamma motor n. fs: innervate the striated part of the intrafusal ms. fs.

Alpha motor n. fs: innervate the extrafusal ms. fs.

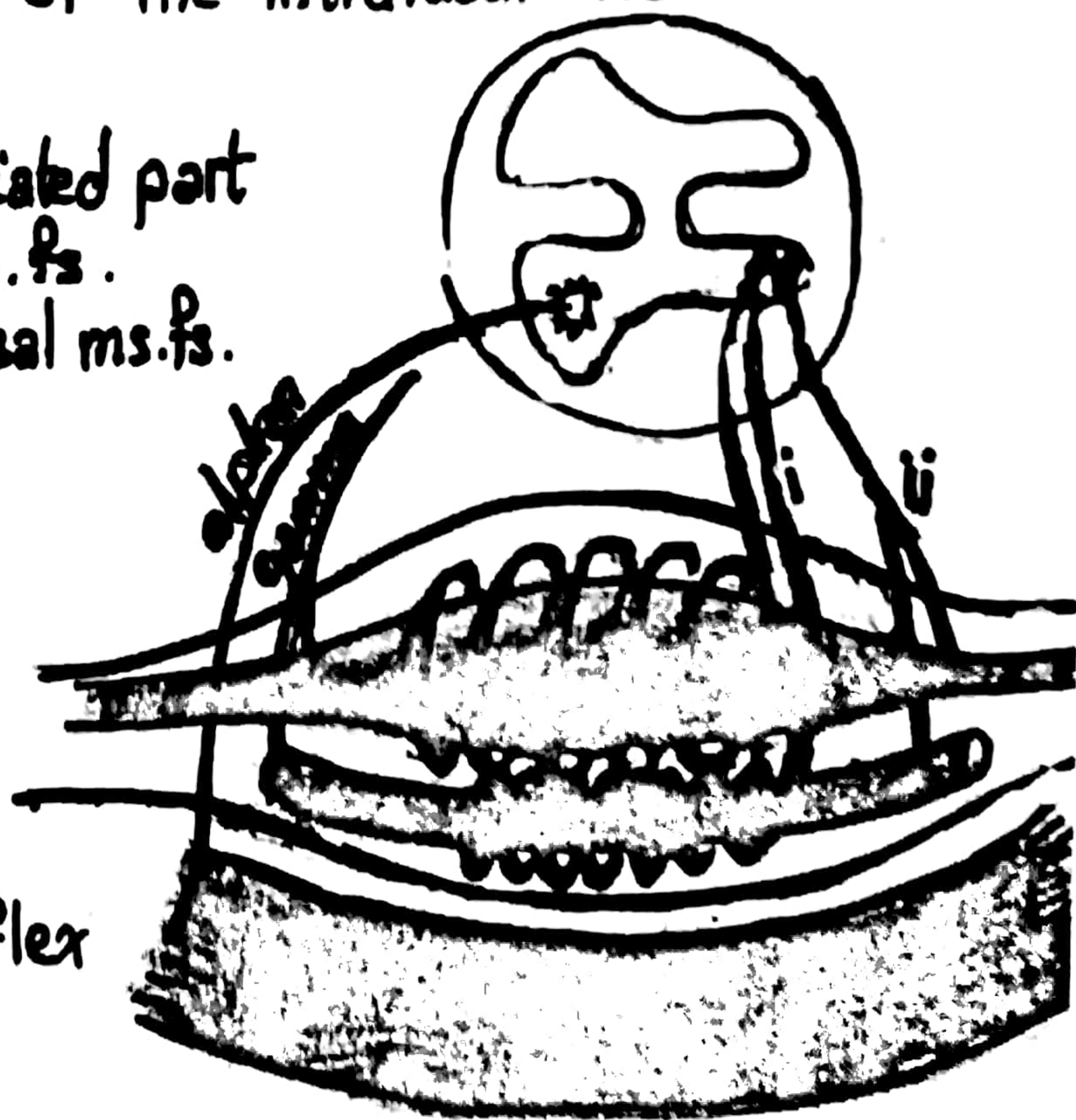
### - Site:

numerous in  
→ to ms. fs.

antigravity muscles.  
ms involved in fine movements e.g.  
intrinsic ms of hand.

### - Function: proprioceptors:

1. regulate ms. tone through stretch reflex
2. Control body posture.
3. Coordinate opposing muscles.





Effector:

# Motor end Plate [Neuromuscular Junction]

The termination of motor nerve on skeletal muscle.

As the motor nerve reaches the muscle, it gives many branches to supply many ms. fs.

As the single n.f. reaches the muscle fibre, it loses its myelin sheath & the neurolemma gradually fuses w' sarcolemma.

The expanded end of the axon = axon terminal rich in mitochondria & synaptic vesicles.

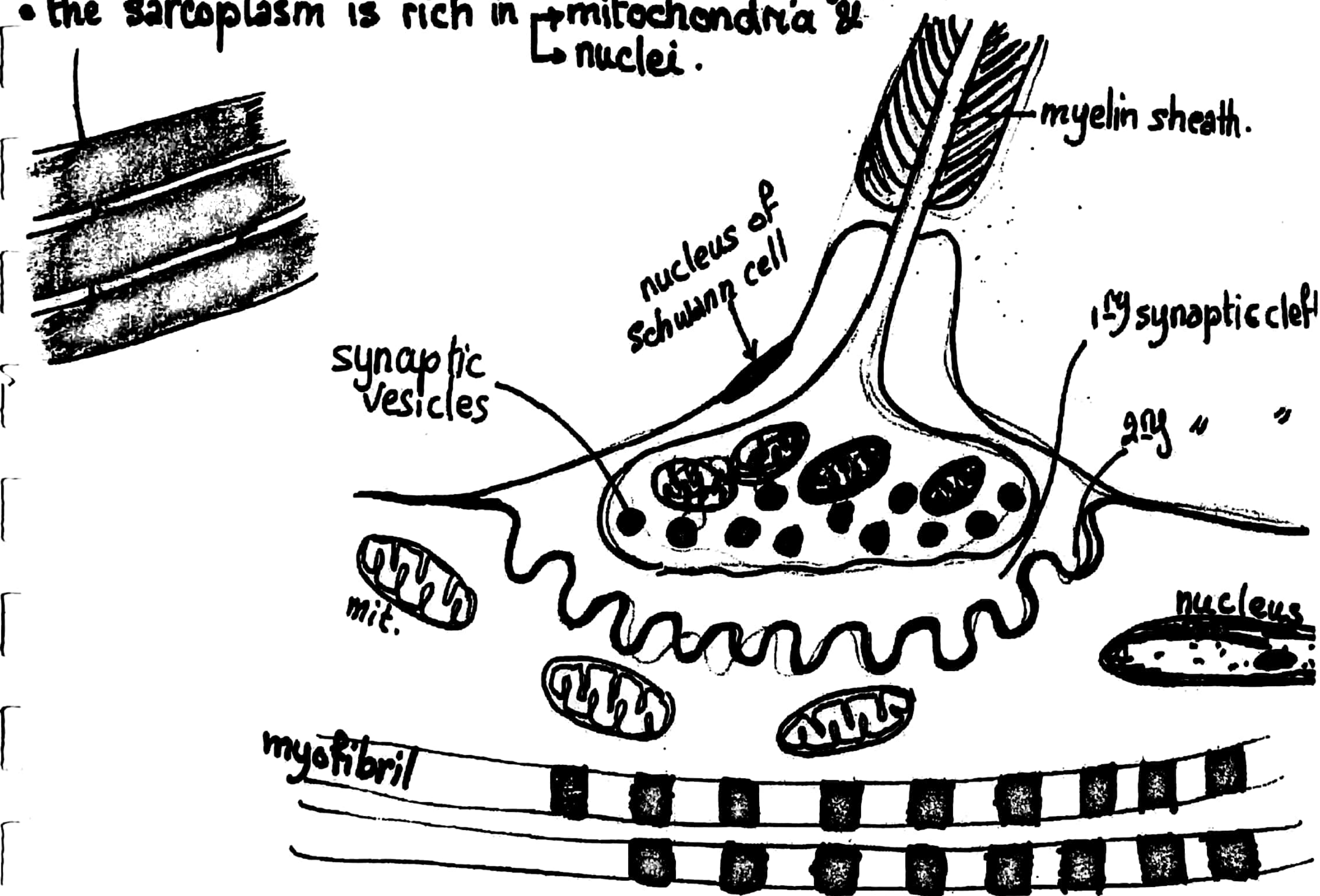
The space bet. the n. fibre & sarcolemma = 1 $\frac{1}{2}$  Synaptic cleft

The sole plate = the underlying depression in sarcolemma & sarcoplasm

It shows the following:

• the post synaptic memb. is folded = 2 $\frac{1}{2}$  synaptic clefts.

• the sarcoplasm is rich in mitochondria & nuclei.





# Blood

-1

def.: A special type of c.t e' fluid matrix (plasma) that circulates inside bl. vs.

Vol.: 5-6 Liters.

weight: 7-8% of body weight.

## Composition:

1. Formed elements (cells) = 45% → red bl. corpuscles (RBCs).  
→ white bl. cells (WBCs).  
→ platelets.

2. Plasma 55%:

90% H<sub>2</sub>O + 7% plasma proteins [albumin, globulin + fibrinogen],  
+ 2% organic subs. e.g. glucose, a.a.s, lipids, enzs, hormones, nitrogen compounds + 1% inorganic salts.

(N.B) Tissue Fluid = plasma that leaves small bl. vs & enter c.t.  
= plasma - plasma proteins.

## Examination:

Blood film: a drop of bl. is spread on a slide, left to dry in air & stained e' a Neutral stain [Leishman] = mixture of eosin (acidic stain), methylene blue (basic) + methyl alcohol [fixative] or

Giemsa & Wright stain: modification of bl. stain by adding azur dyes

Oxidation of methylene blue → new compounds = azures

∴ Azurophilic means metachromatically stained purple e' azure comp

## Functions of Blood:

1. Transport of: O<sub>2</sub>, nutrients, enzs & hormones to tissues & removal of CO<sub>2</sub> & waste products.
2. Protects the body against bact. viruses & antigens.
3. Control: body temp. & acid base balance.

**Red Blood Corpuscles** = [Erythrocytes]

\* **Origin**: Non-nucleated biconcave discs in the b.m. true cells extrude their nuclei & organelles before entering the blood.

\* **Life span**: 120 days

\* **Fate**: Old RBCs are phagocytosed by macrophages in the liver, spleen & b.m. Iron is reused to form new RBCs. Pigments are excreted as bile pigment.

## Osmotic Fragility:

RBCs are isotonic e' plasma [O.P. = 0.9% NaCl (saline)].

Crenation: if put in hypertonic soln. they shrink & show notches.

Hemolysis: " " " hypotonic " " " swell, rupture & the remaining cell memb. = cell Ghost.



## \* Shape:

- In **Surface view**: rounded
- In **Side view**: biconcave: thick at the periphery & thin at the center.  
→ Larger surface area → ↑ capacity for exchange of gases.

## Abnormal Shapes:

- due to change in cell membrane or Hb. content as:  
Spherocytes (spherical), Ovalocytes (oval), Sickle cell (crescent-shape) or poikilocytes (pear-shaped)
- All abn. shapes are fragile → hemolysis → anemia.

## \* Dimensions (size):

Uniform diameter:  $6-9\ \mu\text{m}$  (average  $7.5\ \mu\text{m}$ ).  
Thickness:  $2.2\ \mu\text{m}$  at the edge &  $0.8\ \mu\text{m}$  in the centre.

## Abnormal sizes:

macrocytes: ( $> 9\ \mu\text{m}$ )      microcytes: ( $< 6\ \mu\text{m}$ ) &  
anisocytosis: (different sizes).

## \* L.M.

rounded, non-cleated & acidophilic [as Hb is a basic protein]  
& dark periphery & pale centre (about  $\frac{1}{3}$  of its diameter).

## \* Rouleaux Appearance:

RBCs may adhere to each other → stacked in piles of coins.  
due to the surface tension as they are biconcave in shape  
This process is reversible & no damage to the cells. It occurs only in slow circulation.

## Erythrocyte Sedimentation Rate:

the long chains of RBCs sediment more easily.  
The **ESR** increases non-specifically & inflammation.

## \* E.M.:

Have no nucleus, no organelles. Contain only Hb (electron dense)  
The only organelle is the cell memb. [40% lipid, 50% ptn. & 10% CHO]  
Most of the ptns are integral to maintain their shape. Under the cell memb. a network of filaments (actin, spectrin + memb. associated ptns) this cytoskeleton give the shape & stability of the memb. Also it is flexible & plastic.  
The glycocalyx have sites for bl. groups [ABO, Rh & other groups].

## Hereditary Spherocytosis:

A defect in spectrin gene expression results in: →  
spherical erythrocytes more liable to hemolysis.



## \* Color of RBCs:

- In unstained film their color is due to the Hb.
- In films stained e.g. Leishman: they are acidophilic as Hb = basic ptn. they appear salmon pink e.g. pale centre ( $\frac{1}{3}$  of their diameter) & called **Normochromic RBCs**.

## \* Count of RBCs

By hemocytometer or Electronic Instrument for counting.

## \* Number:

Average  $N^{\circ} = 5$  millions /  $mm^3$  bl. In adult  $\sigma^{\circ} 4.5 - 5.5$  millions /  $mm^3$

In adult  $\phi$  less by  $\frac{1}{2}$  million i.e. = 4-5 millions /  $mm^3$  due to: monthly loss during menstruation + Inhibitory effect of  $\phi$  hormones on the bone marrow. It is highest in newborns & gradually  $\downarrow$ .

## Abn. $N^{\circ}$ :

**I. Polycythemia** =  $\uparrow\uparrow N^{\circ}$  of RBCs  $> 6$  millions /  $mm^3$ . Causes:

1. **False**: hemoconcentration e.g. vomiting, diarrhea, sweating, burn (dehydration)
2. **True**: hypoxia stimulate b.m. to form more RBCs. It may be:
  - **Physiological**: e.g. high altitudes, muscle exercise & newborns.
  - **Pathological**: heart & lung diseases.

**II. Anemia** =  $\downarrow\downarrow N^{\circ} < 4$  millions /  $mm^3$  = **Oligocythemia** or  $\downarrow\downarrow$  Hb conc $^{\circ}$ .

## Causes (types) of anemia:

1. **Deficiency an.**: deficiency of ptn., iron, vit. B<sub>12</sub> or Folic A.
2. **Hemorrhagic an.**: due to excessive loss of blood: acute (accidents) or chronic (bleeding piles).
3. **Hemolytic an.**: excessive destruction of RBCs due to: abn. shape (congenital spherocytosis) or abn. content (as sickle cell & Favism)
4. **Aplastic an.**: bone marrow destruction  $\rightarrow$  pancytopenia [ $\downarrow\downarrow N^{\circ}$  of all bl. cells]
  - $\swarrow$  irradiation
  - $\swarrow$  Chemotherapy
  - $\swarrow$  Idiopathic

**Pernicious Anemia**:  $\downarrow$  vit. B<sub>12</sub>

due to failed production of intrinsic factor in the stomach.

## **Sickle cell anemia:**

Abnormal type of Hb = HbS accumulates at one side  $\rightarrow$  abnormal crescent-shaped RBCs.



**Favism:** hereditary disease due to deficiency of Glucose 6-phosphate dehydrogenase G6PD which is imp. for metabolism of RBCs.

## Functions of RBCs

transport of gases ( $O_2$  &  $CO_2$ ) between tissues & lungs (only within bl. stream)  
Hemorrhage = escape of RBCs outside bl. vs (where they lose their function).

## Adaptation of RBCs to function:

**I. Cell Membrane** → plastic (flexible) → can be squeezed in narrow capillaries.  
→ highly selective → allow only gas exchange (lipoprotein)

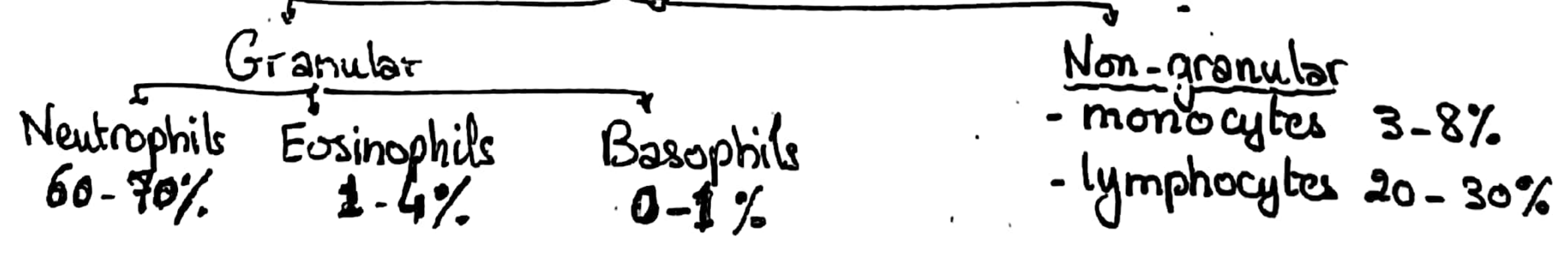
**II. Shape:** → biconcave → ↑ surface area for gas exchange &  
→ have rounded edges → their easy passage in branching vs.

**III. Content:** → No Nuclei or organelles → more space for Hb  
→ contain enzs → Hb reductase [combine e'  $O_2$ ] &  
Hb carbonic anhydrase [ " "  $CO_2$  ].

[33% Hb,  
66%  $H_2O$  +  
1% enzs]

|                              | Erythrocytes [RBCs]                                                         | Leukocytes [WBCs]                                                 |
|------------------------------|-----------------------------------------------------------------------------|-------------------------------------------------------------------|
| Types                        | - 1 type                                                                    | - 5 types                                                         |
| Contents                     | - Not true cells [Corpuscles]<br>No nuclei or organelles<br>contain only Hb | - True cells as they contain<br>nuclei & organelles.<br>but no Hb |
| Colour                       | - greenish yellow                                                           | - colourless.                                                     |
| No                           |                                                                             |                                                                   |
| Diameter                     | - 4.5 - 5.5 millions / $mm^3$ bl. or<br>6-9 (7.5 $\mu m$ )                  | - 4,000 - 11,000 / $mm^3$ bl.<br>- 6-20 $\mu m$ .                 |
| Life span                    | - 120 days                                                                  | - days → years:                                                   |
| Origin                       | - red bone marrow                                                           | - red b.m. & lymphatic tissue.                                    |
| Osmotic pressure & fragility | - Sensitive to changes in osmotic pressure i.e. fragile                     | - more resistant.                                                 |
| Shape & appearance           | - Biconcave disc                                                            | - spherical                                                       |
| movement                     | - Non-motile                                                                | - Motile                                                          |
| Function                     | - carry $O_2$ & $CO_2$                                                      | - Phagocytosis (Defensive)<br>immunity                            |
| Site of function             | - Intravascular                                                             | - Extravascular C.T.                                              |

## Leucocytes





## Leukocytes

General characters of Leukocytes: see the table

- True cells. Colourless in fresh state
- spherical in bl. stream but pleomorphic amoeboid cells in c.t.
- Classified into: Granular & Non-granular according to presence or absence of specific grs.

General Characters of Granular Leukocytes:

- Life span: few days
- Nucleus: single but segmented nucleus e' peripheral heterochromatin & central euchromatin.
- Have 2 types of granules:
  - Azurophil [non-specific] = lysosomes: contain enzs  $\left\{ \begin{array}{l} \text{collagenase} \\ \text{Myeloperoxidase} \\ \text{hydrolase} \\ \text{elastase} \end{array} \right.$  can be metachromatically stained e' azure dye  $\rightarrow$  purple color (as they contain mucopolysaccharides).
  - Specific granules:  
Classified into 3 types according to their affinity to stains.

## Leukocytic Count

I. Total Leukocytic Count = total No of WBCs/mm<sup>3</sup> bl. = 4,000-11,000/mm<sup>3</sup>

Counted by  $\rightarrow$  ① Haemocytometer.

② Electronic counting instrument.

\* Leukocytosis:  $\uparrow\uparrow$  No of WBCs  $> 11,000/\text{mm}^3$

1. physiological: during pregnancy, labour, exercise (transient)

2. Pathological: 1. acute pyogenic infection 2. chronic infection

## Clinical Note

Leukemia = Cancer that starts in the bone marrow  $\rightarrow$  very high count of WBCs & immature cells.

\* Leukopenia:  $\downarrow\downarrow$  No of WBCs  $< 4,000/\text{mm}^3$   
viral infection e.g. influenza or part of pancytopenia (b.m. destruction)

## II. Differential Leukocytic Count:

the % of each type of WBCs to the total No.

Counted in a blood film stained e' Leishman.



# Granular 1

## 1. Neutrophils [Polymorphonuclear leucocytes] PMNs.

% - 60-70 %  
 Diameter - 10-12  $\mu$ m  
 Life span - Few days



**L.M.** → **Nucleus:** single but multilobed 2-5 lobes connected by thin chromatin thread, dark & has many shapes [P.M.N.]

Barr body can be seen in 3-6 % of ♀ cells.

→ **Cytoplasm:** specific granules: numerous fine, pale granules  
 Azurophilic grs.: few, large, stain purple e' azure dye

**Nucleus:** peripheral heterochromatin & small central euchromatin.

**Cytoplasm:** → Have **pseudopodia** (complex cytoskeleton = actin & tubulin)

→ **Few organelles** → Few mit → rich in glycogen → **(E)**  
 small GA  
 few rER

→ **Granules:** 2 types  
 (1) **Azurophilic [1ry]**

• Large, few, dark, considered as 1ry lysosomes: contain:

↓  
 pero-oxidase    acid hydrolase    defensins against bact. fungi & viruses    elastase

(2) **Specific [2ry]**

• small, many & pale. contain:

\* **Collagenase.**  
 \* **Lysozyme:** destroy bact. ptns  
 \* **Lactoferrin:** binds to iron (essential for bact growth)

**actions:** 1st line of defense (non-specific)

ect. toxins attract neutrophils w leave blood & go to C.t. become motile & have pseudopodia [microphages]. In c.t. they:

**Phagocytose bacteria:** azurophil granules fuse e' the phagocytic vesicle

**Secrete contents of specific grs.** → lysis of bact. & c.t.

Lactoferrin binds to iron (essential for bact. growth)

Lysozyme destroys bact. ptns.

collagenase: " collagen so augments movement of neutrophils

**Lead neutrophils → pus cells.**

**Pus ↑↑ body temperature:** stimulates heat regulating centre.

**Attract monocytes to site of infection:** to clean it

**Secrete trephine subs.** → help healing of wounds.

**Stimulate b.m.** → to form more neutrophils.

↑↑ **N°: Neutrophilia** (> 75%) due to Acute Pyogenic infection  
 e.g. Acute tonsillitis, acute appendicitis & abscess.

↓↓ **N°: Neutropenia** (< 60%) → typhoid fever (commonest cause)  
 T.B.



# Eosinophils

## Eosinophils

4-6 %  
- 14 µm  
few days



N. bilobed connected by chromatin thread.  
in large refractile acidophilic specific granules.

Peripheral heterochromatin & central euchromatin than neutrophil.  
few organelles.

types of granules:

**hil** • small, round = lysosomes  
**fic**: oval & electron crystalline core of basic ptn dense periphery containing  
- histaminase &  
- sulphatase

secrete Histaminase & sulphatase destroy histamine & heparine of the allergic reaction  
phagocytose antigen-Ab complex & against parasites:  
toxic effect of basic ptns  
hydrolytic enzs of azurophilic grs.

**Eosinophilia** > 5%

allergic diseases: Urticaria, eczema, bronchial asthma  
infective: Bilharziasis.

**Eosin** 1%

## 3. Basophils

- 0-1 %  
- 10-12 µm  
- few days



N. Irregular, segmented → <sup>pale</sup> S-shaped.  
C Coarse basophilic granules w obscure the nucleus. metachromatically stained e' Toluidine blue → purple.

N. has minimal peripheral heterochromatin & more central euchromatin

C. few organelles

+ 2 types of granules:

• **Azurophilic**:  
small = lysosomes

• **Specific grs**:  
large, rounded, electron dense & contain:  
→ Histamine  
→ Heparine  
→ eosinophil chemotactic factor  
→ Leukotrienes.

Cell memb. shows receptors for Ig E.

## Functions

1. Secrete **Heparine** [prevent clotting & promotes allergy]
2. Secrete **Histamine** → vasodilatation  
→ sudden ↓ in bl. press → anaphylaxis
3. Attract eosinophils to site of allergy by **Eosinophil chemotactic factor**
4. **Leukotrienes** → bronchospasm  
→ bronchial asthma.
5. limited phagocytic power

## ↑ No = Basophilia

1. Allergic diseases.
2. Parasitic "
3. viral infection [chicken pox].



## Non-Granular leucocytes

Have no specific granules, but small azurophil granules & rounded or indented N.

### Lymphocytes

### I Monocytes

### Monocytes

% : 3-8%      • diameter : 14-20  $\mu$ m

life span : 3 days in bl. & 3 months in c.t.

L.M. : N. : large, eccentric, kidney-shaped, pale e' 1 or 2 nucleoli.

C. : non-granular, non-clear pale basophilic (bluish grey). Has frosted glass appearance due to lysosomes (azurophil gr).

E.M. :

N. minimal condensed chromatin e' central extended chromatin & clear nucle.

C. have pseudopodia, mit, rER, well developed G.A. & centrioles in the concavity of the N. + many lysosomes [15 & 25].

Functions : Highly phagocytic cells :

1. remain in blood for 3 days then →
2. enter c.t. & change into macrophages to phagocytose bact. & debris
3. Antigen presenting cells.
4. The precursors of all phagocytic cells : e.g dust cells of lungs, Kupffer cells of liver, osteoclasts of bone & microglia of CNS.

Monocytosis :  $\uparrow\uparrow$  % > 8% due to chronic infections; T.B., Syphilis, glar fe  
↳ monocytic leukemia.

Monocytopenia :  $\downarrow\downarrow$  e' glucocorticoids & part of pancytopenia.

### II Lymphocytes 20-30%

• 2<sup>nd</sup> most common cell of WBCs      • 2<sup>nd</sup> line of defense

• The functioning unit of specific immune response.

• Immune competent cells : Have surface markers (receptors) for antigens.

$\uparrow\uparrow$  N° = lymphocytosis : > 30%      ↳ physiological in children  
↳ chronic infect<sup>ns</sup> e.g. T.B, whooping Cough  
↳ Leukemia.

$\downarrow\downarrow$  N° = lymphocytopenia (pancytopenia)

| diameter: (2 types)      Small                                                       | Large                                                                 |
|--------------------------------------------------------------------------------------|-----------------------------------------------------------------------|
| %      15-20% of WBCs                                                                | - 5-10%                                                               |
| diameter: 6-8 $\mu$ m                                                                | - 10-15 $\mu$ m                                                       |
| <u>L.M.</u> : N. : dark & filling the cell                                           | N. large, indented, pale e' clear nucleolus                           |
| C. : little, pale basophilic rim around the nucleus                                  | C. abundant, deeply basophilic.                                       |
| <u>E.M.</u> N. e' condensed heterochromatin                                          | N. less condensed e' prominent nucleol.                               |
| C. few mit., small GA, many Free ribosomes + 2 centrioles + small azurophil granules | C. abundant, more organelles : mit., ribosomes, rER, G.A. + lysosomes |

**Large lymphocytes** = either activated lymphocytes (or) Natural Killer cells.

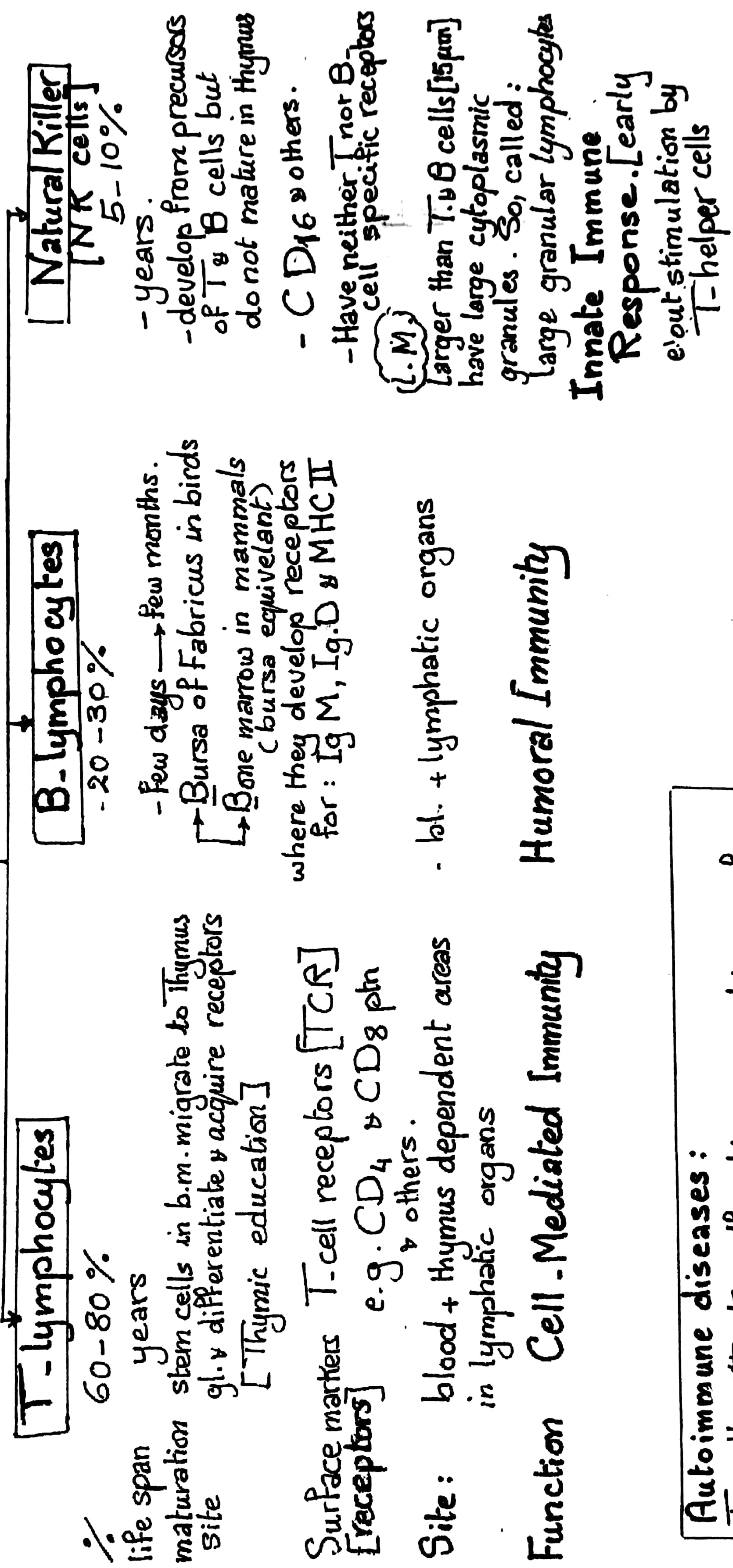


**Motility & distribution**: actively mobile, continuously circulating bet. the bl. & lymphatic organs. where they settle they are the only cells w can return to blood. ∴ Found in: bl., lymph + lymph. tissue.

## Classification of lymphocytes

Cannot be differentiated by L.M. or E.M. They differ only in the surface receptors  
Can only " " " immunohistochemical staining. ∴ 3 types according to function

### lymphocytes



**Autoimmune diseases:**  
T-cells attack self antigens, so tissues of the patient are destroyed by his own T-cells



## Functions

### T-lymphocytes

#### Types: Cytotoxic $CD_8^+$ T-cells:

F:  $\rightarrow$  cell-mediated immunity.

Specificity: Antigen in virus infected or neoplastic cells bind to MHC I  $\rightarrow$  Ag-MHC I complex.

Mode of action:

When the Ag-MHC I complex binds to receptors on Cytotoxic  $CD_8^+$  T-cells, they proliferate, become active effector cells that secrete lymphokines & perforins  $\rightarrow$  channels in cell memb. of the cells directly killing them. ② Contribute in graft rejection.

#### ②. Helper $CD_4^+$ T-cells:

F:  $\rightarrow$  induction of immune response to an antigen.

Specificity: Ag. phagocytosed by antigen presenting cells [APC, e.g. macrophages & B-cells] & bind to MHC II  $\rightarrow$  Ag-MHC II complex.

Mode of action:

When the Ag-MHC II complex binds to receptors on Helper  $CD_4^+$  T-cells, they secrete interleukin II  $\rightarrow$  stimulate proliferation of more helper cells. They secrete lymphokines & stimulate T & B-cells.

#### ③. Regulatory (Suppressor) T-cells:

F: 1. Suppress the immune response to self antigen. 2. Switch off " " " to foreign Ag when it is removed.

Mode of action: Suppress cellular immunity by T-cells, suppress T-helper cells controlling humoral immunity.

#### ④. Memory T-cells:

F: rapid response of T-cells on re-exposure to the same Ag. [2<sup>nd</sup> immune response]. They are either  $CD_8^+$  or  $CD_4^+$ .

### B-lymphocytes

#### Humoral Immunity:

Mode of action:

When the sp. Ag. binds to receptors on B-cells  $\rightarrow$  receptor mediated endocytosis & fragments of the Ag. bind to MHC II molecules.

1. helper cells bind to Ag-MHC II complex on the B-cells, become active & secrete cytokines [IL II] & stimulate proliferation & differentiation of B-cells.

Activated B-lymphocytes either:

1. change into plasmablasts then plasma cells that form & secrete antibodies.

2. give B-memory cells:

responsible for the rapid response on the 2<sup>nd</sup> exposure to the same Ag.

#### Memory Cells

Can survive  $\geq 20$  years  $\rightarrow$  life long immunity in the absence of the Ag. This is the principal of Vaccination.

#### HIV human Immunodeficiency

virus that causes AIDS destroy  $\rightarrow$  T-helper cells  $\rightarrow$   $\downarrow$  immunity & becomes susceptible to opportunistic infections & do not infect normal persons.

### Natural Killer

#### [NK cells]

Cytotoxic lymph.

① Identify & directly kill transformed cells (similar to cytotoxic  $CD_8^+$  T cells)

② Secrete Antiviral agent [Interferon]

#### Identification of

NK cells for transformed cells:

The presence of

MHC I prevents killing of healthy cells by NK cells

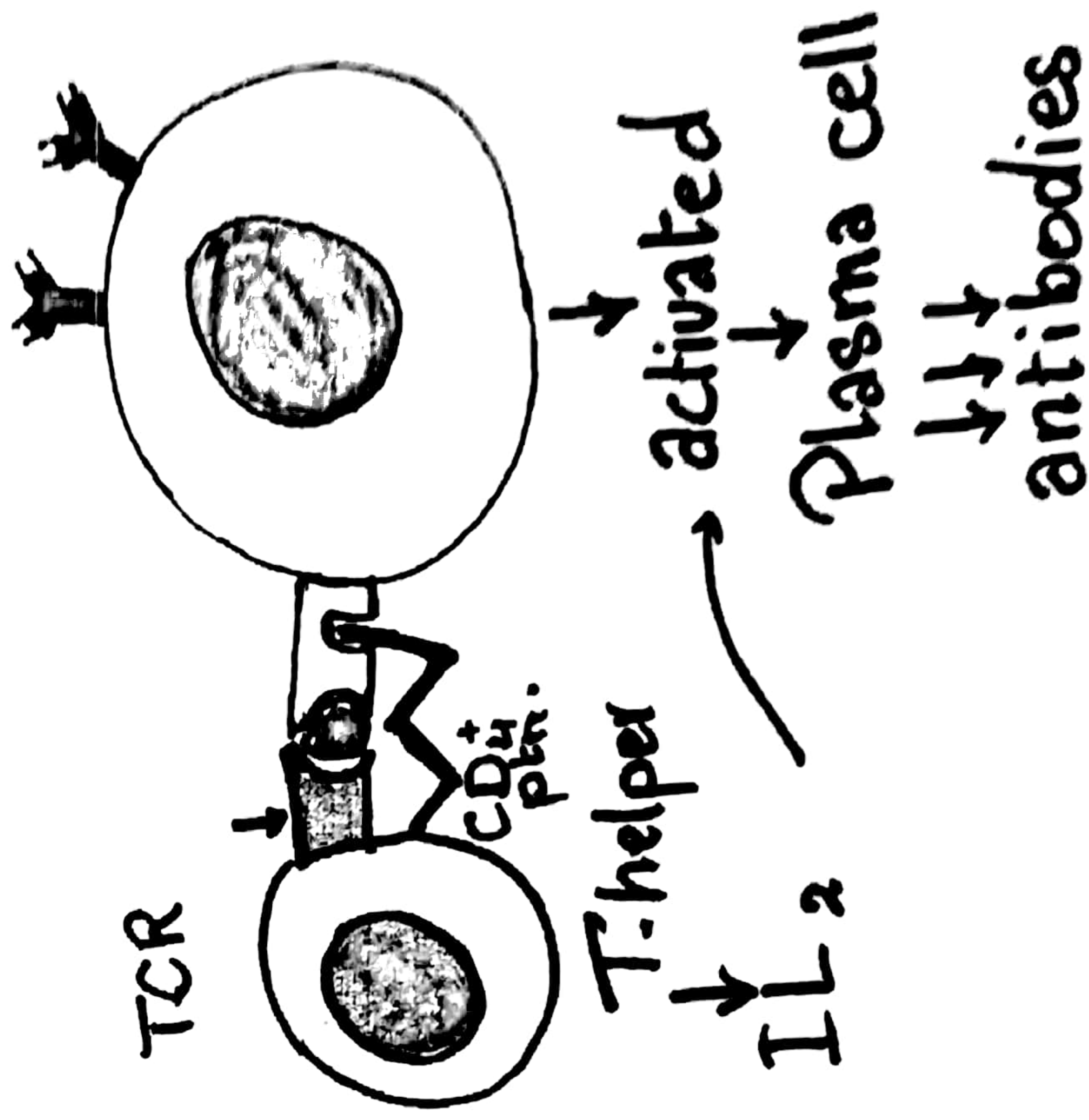
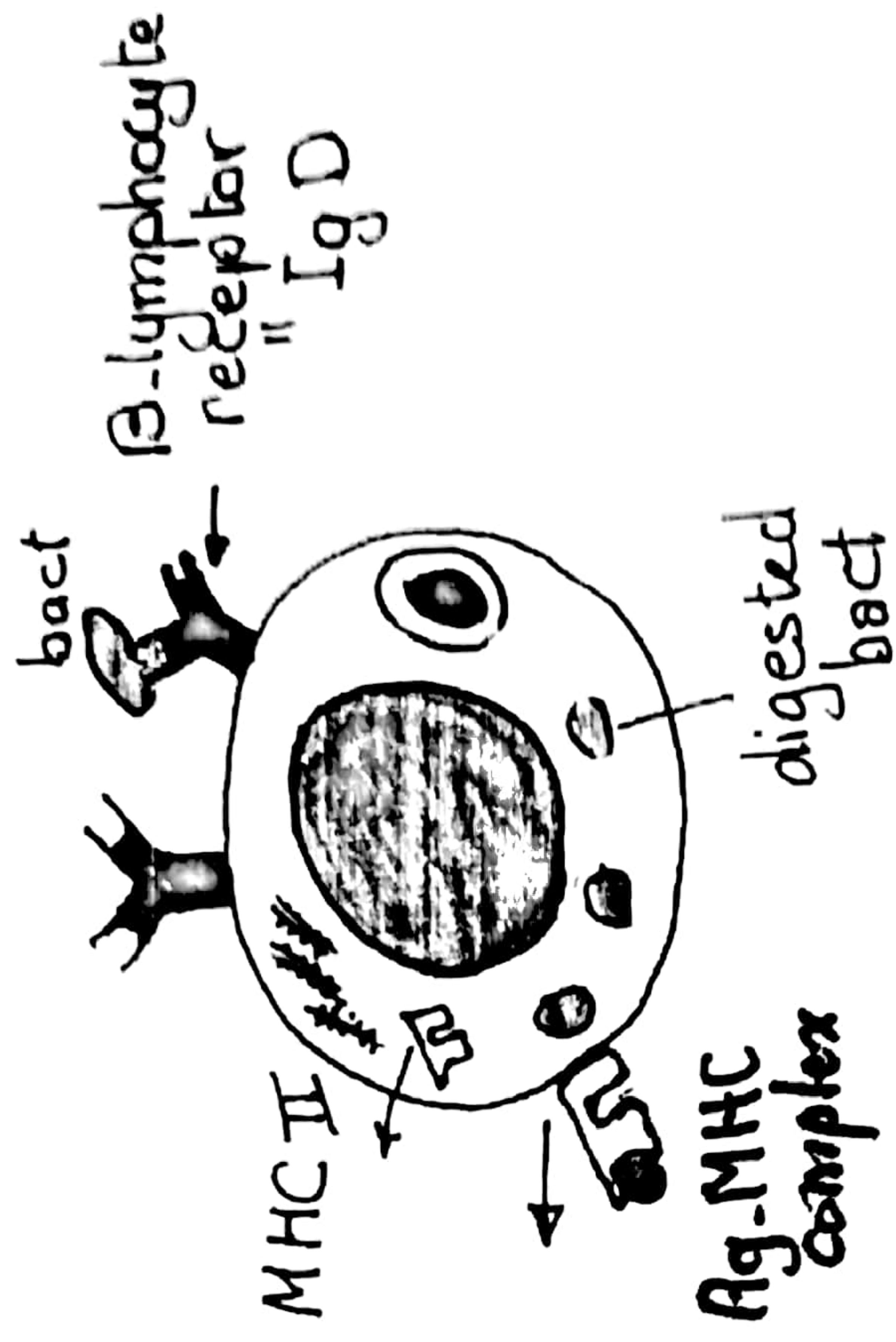
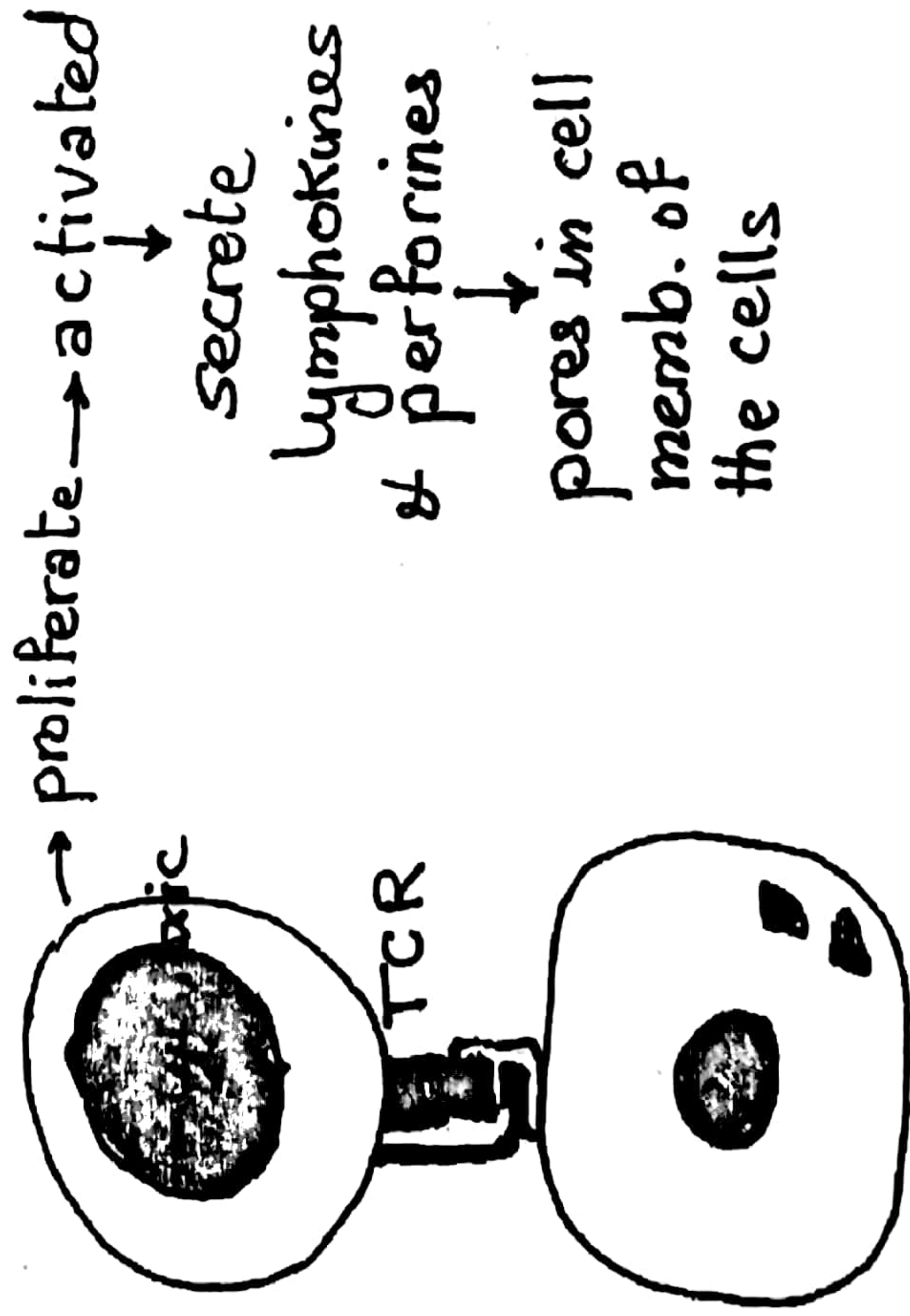
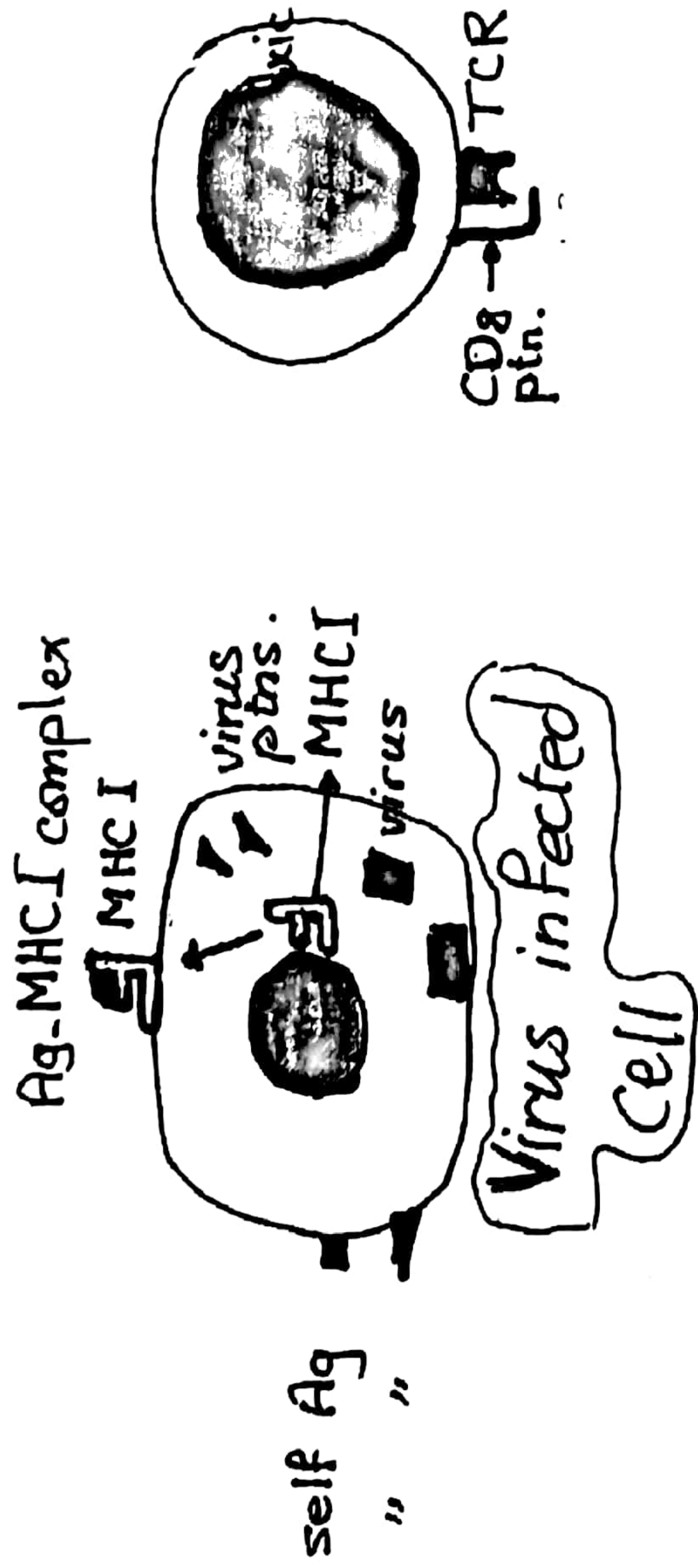
Neoplastic & virus-infected cells suppress MHC I

(N.B) transformed cells

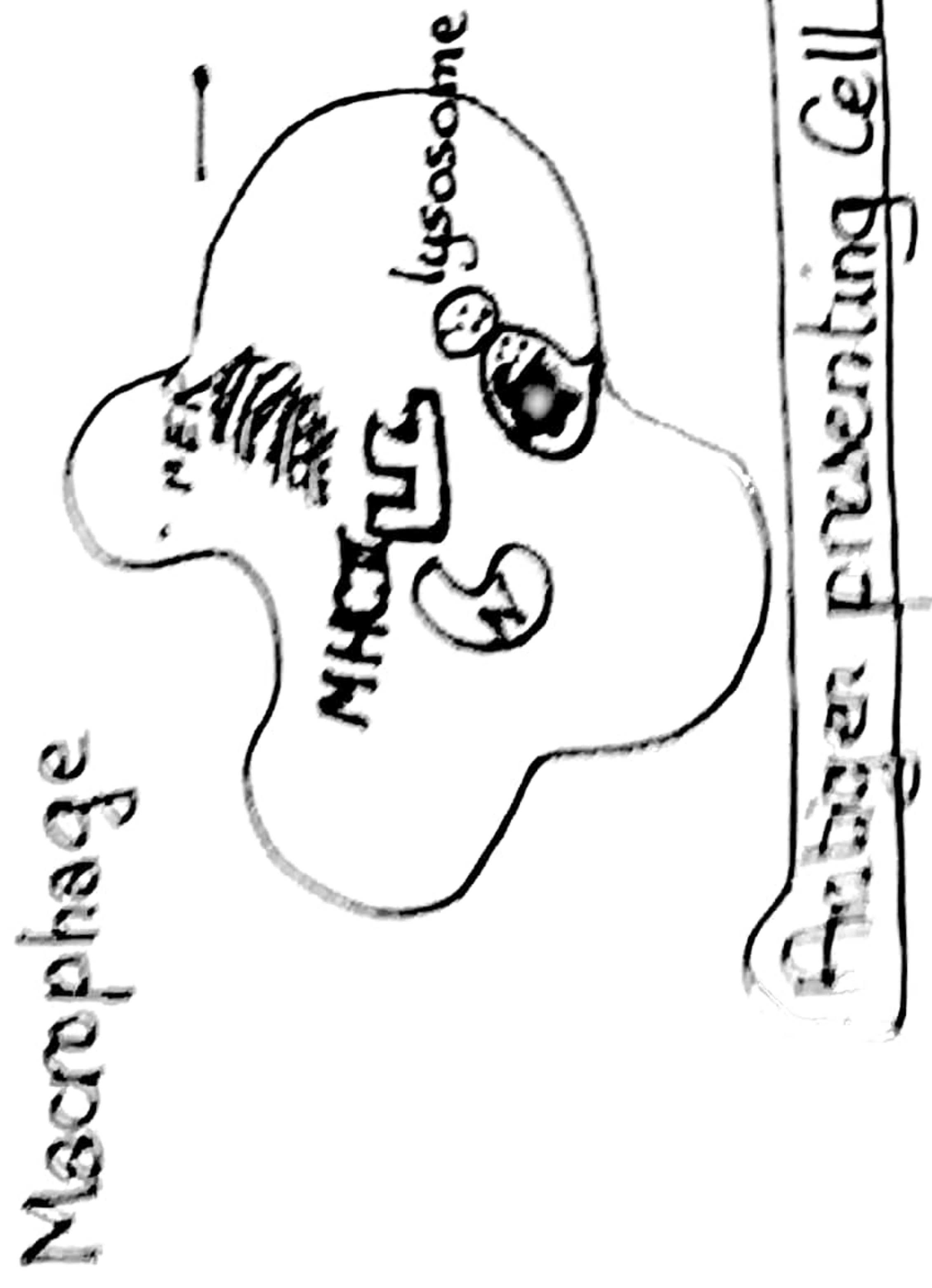
Tumor cells, virus-infected cells, fungi & parasites.



# Cytotoxic T-lymphocytes.







When Ag binds to MHC II

→ Ag-MHC II complex binds to receptors on T-helper cells

↓ IL II

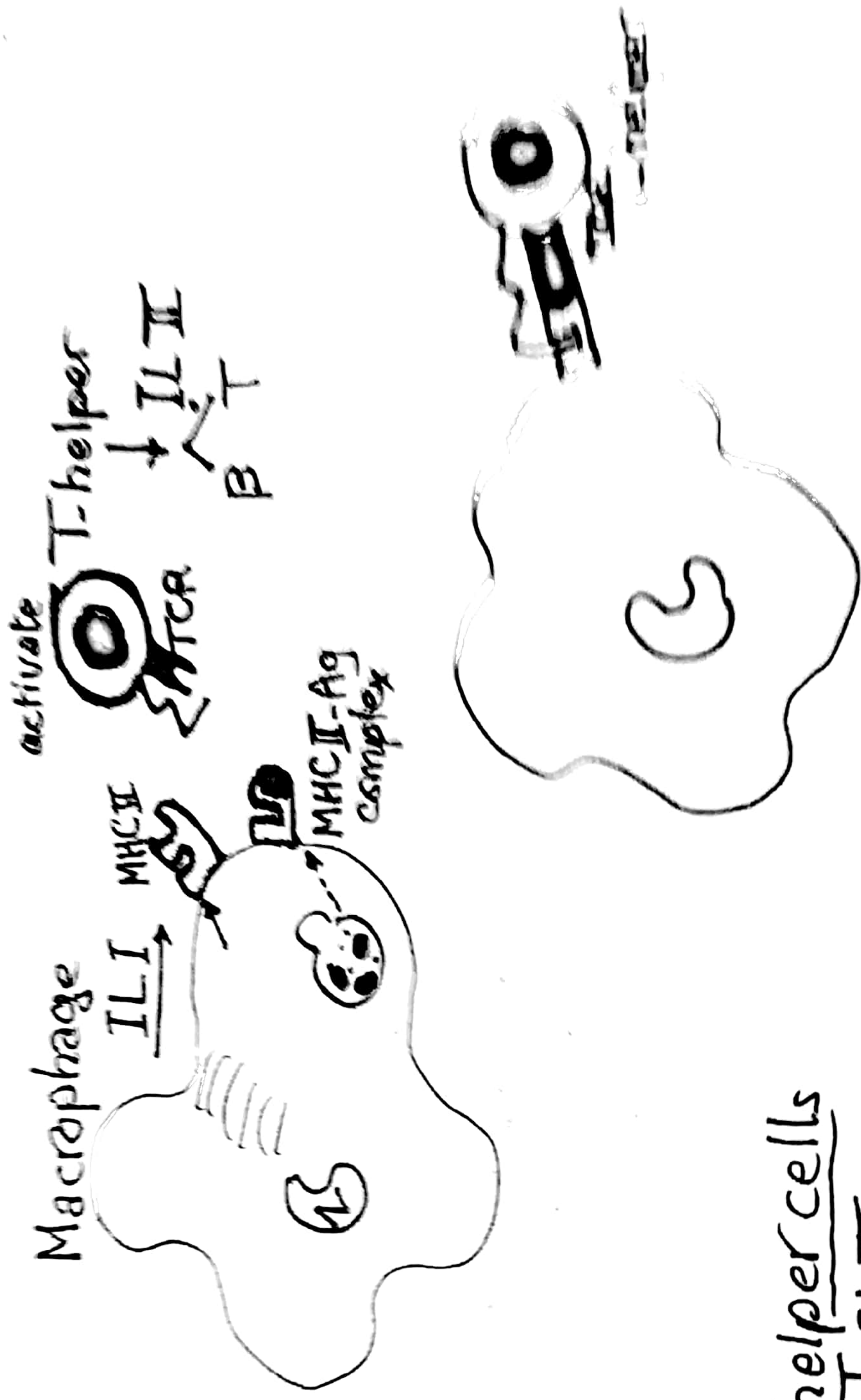
proliferation of more helper cells  
→ secrete lymphokines

stimulate

→ B-lymphocytes

→ T-lymphocytes

→ NK cells





# Platelets [thrombocytes]

all non-nucleated cytoplasmic fragments.

origin: develop from megakaryocyte.

count:  $200,000 - 400,000 / \text{mm}^3$

size:  $2 - 4 \mu\text{m}$

shape: oval, non-nucleated fragments w have 2 zones:

outer pale basophilic (clear) peripheral zone = Hyalomere.

inner dark granular zone = granulomere.

1:  
the cell memb. have thick cell coat that help aggregat<sup>n</sup> of platelets  $\rightarrow$  clumps.

hyalomere: contains cytoskeleton:

$\rightarrow$  microtubules } maintain cell shape.  
actin filaments }

open canalicular system: invaginations of cell memb. to release serotonin

$\rightarrow$  facilitate uptake of fibrinogen from the plasma

dense tubular system: store for  $\text{Ca}^{2+}$ , do not communicate w the surface  
have dense material

granulomere: contains:

few mit., ribosomes, <sup>(energy)</sup>glycogen & 3 types of granules:

1.  $\alpha$ -granules: contain clotting factors & growth factors.

2. Delta [Dense] granules: contain serotonin, ATP, ADP

3. Lambda granules = lysosomes.

functions:

Platelet aggregation  $\rightarrow$  platelet plug to stop bleeding.

secrete serotonin  $\rightarrow$  vasoconstriction.

Form bl. clot or thrombus: platelets deposit network of fibrin threads  
 $\rightarrow$  trap bl. cells [bl. coagulation].

Clot retraction: contraction of platelet microfilaments.

Clot removal: after healing of bl. vs., the clot is removed by lysosomal  
& plasmin (proteolytic enz) in lambda granules.

Purpura = thrombocytopenia:

No of platelets  $< 50,000 / \text{mm}^3$  due to  $\rightarrow$   $\downarrow$  production [b.m. depression] or  
 $\rightarrow$   $\uparrow$  breakdown [autoimmune dis]

characterized by:

prolonged bleeding time

excessive bleeding after minor trauma.



# In Hyperallergic Individuals :

2<sup>nd</sup> exposure to the same Ag → degranulation of large N<sup>o</sup>. of Basophils & mast cells → wide spread vasodilatation → ↓↓ in bl. vol. → Shock.

Contraction of smooth muscles of the bronchial tree → resp. insufficiency.

A condition called Anaphylactic shock (life threatening).

## Comparison between Basophils & Mast cells 5

|                  | Basophils                                           | Mast cells                |
|------------------|-----------------------------------------------------|---------------------------|
| Diameter         | - 10 - 12 μm.                                       | - 20 - 30 μm.             |
| life span        | - few days.                                         | - weeks → months (longer) |
| Nucleus          | - segmented.                                        | - rounded.                |
| Phagocytic power | - slightly phagocytic.                              | - not phagocytic.         |
| granules         | metachromatic & contain Heparin, histamine & others |                           |
| Receptors        |                                                     |                           |
|                  | receptors for Ig E                                  |                           |



# Haemopoiesis

Formation of blood cells in:   
 → bone marrow &   
 → lymphatic organs e.g. thymus.

**Bone Marrow** = [Myeloid tissue]   
 2 types

| Red Bone Marrow (active)                                                      | Yellow Bone Marrow (inactive)                                                                                                                               |
|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|
| present in most bones of children<br>in adults: flat, short & irregular bones | - a store for fat (occupy $\frac{1}{2}$ the space)<br>- in shafts of long bones of adults<br>- can change into active on need<br>e.g. after severe bl. loss |

## Structure of red b.m.

### 1. Stroma:

- **Fixed cells**: reticular cells, together e' reticular fibres → network in the background + fibroblasts, UMC, pericytes, osteogenic cells & Fat cells (the largest cells in b.m.).

### - Blood sinusoids:

Wide irregular bl. capillaries lined e' endothelial cells e' non-continuous basement memb. through their pores bl. cells leave to the blood. (only mature cells)

### 2. Free Cells:

#### • Developing stages of the blood cells.

the ratio of immature WBCs to immature RBCs = 5:1 as the life span of <sup>most</sup> WBCs is shorter than that of RBCs.

#### • Stem Cells:

1] **Pluripotential Stem Cells** = mother cell of all blood cells = CFU

2] **Multipotential Stem Cells**:

2 types   
 → **Common Myeloid Stem cells** [CFU-GEMM]   
 → CFU-Granulocytes   
 → CFU-Erythrocytes   
 → CFU-Monocytes   
 → CFU-Megakaryocyte.   
 → **Common Lymphoid stem cells** [CFU-Ly] → give the 3 types of lymphocyte

3] **Restricted progenitor cell** = unipotential, restricted or committed to form 1 line of cells

e.g. CFU-E, CFU-G, CFU-M, CFU-megakaryocyte.

1, 2 & 3 are similar to small lymphocyte but e' pale nucleus.

4] **Blast cells**: give rise to mature cells. (not self renewing)

• Diff. types of stem cells are not distinguished by L.M. but identified by immunocytochemical staining of their diff. markers.



- Bone marrow Aspiration or biopsy is stained e' Wright-Giemsa to diagnose disorders e.g. aplastic anemia or leukemia.

## BM transplantation [donation]

In b.m. diseases e.g. leukemia, hemopoietic stem cells taken from a donor are infused into the same person (autologous) or another person (allogenic).

## Erythropoiesis

- ① Pluripotential stem cells: CFU  
= Stem cell for all blood cells → common myeloid stem cell. CFU.GEMM  
Under control of erythropoietin will give →
- ② CFU.E = restricted erythrocyte progenitor.
- ③ Pro-erythroblast: the 1st recognizable cell in b.m.  
Largest cell ( $17\mu\text{m}$ ) e' large pale nucleus e' prominent nucleoli & pale basophilic cytoplasm.
- ④ Basophilic erythroblast:  
the cell becomes smaller ( $15\mu\text{m}$ ). Nucleus: smaller & darker.  
Cytoplasm: deeply basophilic (rich in ribosomes & polysomes).
- ⑤ Polychromatophilic erythroblast: (the last cell to divide)  
the cell becomes smaller ( $13\mu\text{m}$ ). Nucleus: smaller & darker.  
Cytoplasm becomes violet as it takes both basic (ribosomes & polysomes) & acidic stains (Hb).
- ⑥ Normoblast: (orthochromatophilic)  
The cell becomes smaller ( $11\mu\text{m}$ )  
Nucleus: becomes smaller, darker & eccentric to be expelled outside.  
Cytoplasm is acidophilic (Hb).
- ⑦ Reticulocyte:  
- The cell become smaller [ $9\mu\text{m}$ ]  
- Cytoplasm: Acidophilic (Hb) e' remnants of ribosomes & polysomes that form reticulum.  
- In peripheral blood: its % does not exceed (1%)  
- Their % ↑↑ in case of Haemorrhage or destruction of RBCs.  
- Can be stained by supravital stain = Brilliant Cresyl Blue.

## ⑧ Mature RBCs



# Granulopoiesis

[development of Granular WBCs]  
[stimulated by colony stimulating factors]

- ① Pluripotential stem Cell = CFU. = [colony forming unit] → CFU.GEMM  
stimulated by ← Colony stimulating factor
- ② CFU-granulocyte: CFU.G.
- ③ Myeloblast: earliest recognizable precursor  
Large cell. N. large, rounded & prominent nucleoli.  
Cytoplasm: pale basophilic.
- ④ Promyelocyte: (largest cell)  
↑↑ size (20 μm). Have darker nucleus but prominent nucleolus  
Have pale basophilic cytoplasm  
E.M: mit., rER, G.A. + azurophil granules = lysosomes.
- ⑤ Myelocyte: [N., E. & B.]  
- The cell becomes smaller, The Nucleus: becomes darker & indented.  
- Specific granules start to appear, so it differentiates into 3 types
- ⑥ Metamyelocyte: [N, E. & B]  
- Cannot divide. differentiate by metamorphosis.  
- the cell become smaller. N. more condensed & more indented →  
[Kidney-shaped]. Specific granules ↑↑ in No.  
- Neutrophil metamyelocytes are called Juvenile Neutrophils.
- ⑦ Band (Staff) or Stab form:  
- The cell become smaller. N. more condensed & more indented →  
(curved rod). Specific granules ↑↑ in No.  
- Their % in peripheral blood do not exceed 2%.  
- If % ↑↑ It indicates severe acute infection.
8. Mature Neutrophil, Eosinophil & Basophil:



# Development of Monocyte,

- 4 -

- ① Pluripotential stem cell = CFU.  $\rightarrow$  CFU - GEMM  $\xrightarrow{IL}$
- ② CFU. monocyte [CFU-M] = restricted monocyte progenitor.
- ③ Monoblast : similar to myeloblast.
- ④ Promonocyte : very large e' large indented nucleus & basophilic cytoplasm.
- ⑤ Monocyte

## Development of lymphocytes

- ① Pluripotential stem cell [CFU].
- ② CFU. lymphocyte.  $\downarrow$  cytokines
- ③ lymphoblast : similar to other blasts.
- ④ Prolymphocyte :  
Smaller e' darker nucleus  
either  $\rightarrow$  remain in B.M. & give B-lymphocytes.  
or  $\rightarrow$  migrate to thymus & " T-lymphocytes  
or  $\rightarrow$  appear in circulation as NK-cells.

## Development of platelets Thrombopoiesis

- ① Pluripotential stem cell CFU.  $\rightarrow$  CFU-GEMM  $\xrightarrow{IL}$
- ② CFU. Megakaryocyte [CFU-Meg] = restricted megakaryocyte-progenitor
- ③ Megakaryoblast : similar to other blasts but e' indented nucleus  
last cell that can divide
- ④ Promegakaryocyte : (45  $\mu$ m)  
larger cell e' larger multilobed N. e' basophilic cytopl. e' many azurophilic granules
- ⑤ Megakaryocyte : [50-70  $\mu$ m]  
Have single multilobed dark N & basophilic cytopl.  
Invaginations of cell memb  $\rightarrow$  demarcation channels dividing the cytoplasm  
into fragments that shed as platelets. Also it extends pseudopodia  
(platelet ribbons) from w platelets detach.

|          | Megakaryocyte      | Osteoclast                        |
|----------|--------------------|-----------------------------------|
| Site     | Bone marrow        | Howship's lacuna on bony surfaces |
| Diameter | 50-70 $\mu$ m      | 150 $\mu$ m                       |
| Cytopl.  | basophilic         | Foamy acidophilic                 |
| Nucleus  | Single, multilobed | Multinucleated                    |
| Function | form platelets     | bone resorption.                  |



Large elastic arteries | e.g. **Aorta** & large branches  $\leftarrow$  subclavian art. 1.  
pulmonary a.

- Have thick wall, yellow in fresh section. (mainly formed of elastic Ps)
- Have wide lumen. formed of:

### I. Tunica Intima:

- a. Endothelium : s.sq. epith.
- b. subendothelial c.t. rich in elastic fibres, long. collagen fs + fibroblasts.
- c. undifferentiated int. elastic lamina (similar to elastic laminae in t.med)

II. Tunica Media: [70% of the wall]

= 40-70 laminae of fenestrated elastic membranes (↑↑ e' age)

Penestrae facilitate diffusion of substances through the arterial wall.

+ Circular smooth muscles. w produce the elastic fibres & ground subs.  
collagen "

### III. Tunica adventitia: [20%]

1. Tunica adventitia: [20%]  
thin = loose c.t. & contains: longitudinal collagen fibres + elastic fibres +  
Vasa Vasora + nerves & lymph vessels.

(N.B.) During Systole, large elastic arteries distend while during diastole, their elastic recoil  $\rightarrow$  regains their original size & push bl. to smaller arteries.

**Med. Sized artery** = muscular artery (see table)

deliver bl. to organs.

| Large Elastic Artery                                                                                                                                                                                                                                                                                    | Med. sized Muscular artery                                                                                                                                                                                  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>site - Aorta &amp; its branches e.g. pulmonary</p> <p>T. Intima - Thicker<br/>undifferentiated int. elastic l.<br/>(not prominent)</p> <p>T. media - mainly elastic laminae &amp;<br/>smooth muscles in bet.<br/>undifferentiated Ext. Elastic l.</p> <p>T. adventitia - presence of Vasa Vasora</p> | <p>- most muscular &amp; organ as</p> <p>- thinner<br/>prominent IEL.</p> <p>- mainly smooth ms &amp; elastic &amp; collagen fs in bet.</p> <p>- prom. E.E.L. in some arteries</p> <p>- no Vasa Vasora.</p> |

## Specialized Med. sized arteries:

|           | basilar art.                            | Coronary a.                                                  |
|-----------|-----------------------------------------|--------------------------------------------------------------|
| T. Intima | thick, prominent<br>Int. elastic lamina | thick, contains: long. sm. ms, fat<br>droplets IEL: present. |
| T. Media  | - Thin                                  | - Thick.                                                     |
| T. adv.   | - Thin.                                 | Ext. elastic lamina<br>separates it from T. media            |



| Med. sized artery                                                               | Med. sized vein                                                   |
|---------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1. Thick wall & narrow lumen                                                    | - Thin wall & wide lumen                                          |
| 2. rounded lumen & do not collapse                                              | - flat lumen & collapse after death                               |
| 3. No valves                                                                    | - Have valves.                                                    |
| 4. No bl. after death.                                                          | - contains bl. after death.                                       |
| 5. <u>T. intima</u> : thick, folded, rich in elastic fs + clear int. E. lamina. | - thin, not folded, poor in elastic fs<br>no int. elastic lamina. |
| 6. <u>T. Media</u> : thick, rich in elastic fs.                                 | - thin = sm.ms, poor in elastic fs.                               |
| 7. Ext. elastic lamina may be present                                           | - No ext. elastic lamina.                                         |
| 8. <u>T. Adventitia</u> : thin, rich in elastic fs                              | - thick, rich in collagen fs.                                     |
| 9. Has rapid flow of arterial bl.                                               | - slow flow of venous blood                                       |

## Small arteries = Arterioles

< 100  $\mu\text{m}$  in diameter. gradually ↓ in diameter if < 50  $\mu\text{m}$  = Terminal arterioles

↳ control bl. flow to capillaries

↳ responsible for peripheral resistance of bl. vs. Formed of:

T. intima: v. thin (thin c.t) & thin IEL w gradually disappears in smaller arteriole

T. media: 1 or 2 layers of sm.ms " " " " & replaced by pericyte

T. adv.: v. thin

↑↑ tone of sm.ms. of t. media of arterioles → hypertension

## Metarterioles:

= lat. branches of terminal arterioles = connections bet. arterioles & capillaries.  
surrounded by rings of sm.ms w act as sphincters to control blood flow to the capillaries.

Aging → subendothelial deposition of lipids & Ca → atherosclerotic plaque → loss of the integrity of the arterial endothelium.



## Veins

- 1] Small veins = Venules into w capillaries drain : = [post capillary Venules]  
 Very thin walled [20-30  $\mu\text{m}$ ] in diameter  
T. intima: endoth. resting on thin b.m.  
T. Media: = pericytes. & as the diameter  $\uparrow$  smooth ms start to appear  
T. adv.: thick.

(N.B) Exchange of materials bet. bl. & tissues occurs in  $\rightarrow$  capillaries &  $\rightarrow$  post cap. venules.

## 2] Med. sized veins [muscular]: (see the table)

- T. intima: endoth, subendoth c.t. (thin) e' no int. elastic L.  
T. media: circular sm. ms. + longitudinal collagen fs, fibrobl. few elastic fibres  
T. adv. thick = loose c.t. rich in collagen fs.

(N.B) Valves = folds projecting from T. intima formed of elastic c.t. covered e' s.sq. endothelium. Absent in small & large veins

## 3] Large Veins: e.g. inf. Vena Cava:

Have thick wall & wide lumen

- T. intima: no IEL, Have valves.

- T. media: thin

- T. adventitia: thick = loose c.t. contains long. smooth ms to facilitate elongation & shortening of I.V.C. e' respiration.

## Arterio-Venous Connections [peripheral Circulation]

### I Blood Capillaries

Narrow vessels formed by rolling of endothelial cell resting on a basal lamina w splits to enclose pericyte.

length: < 50  $\mu\text{m}$  . diameter 8-10  $\mu\text{m}$ .

Pericytes  $\rightarrow$  Have contractile function  $\rightarrow$  regulate bl. flow in caps.

$\rightarrow$  can differentiate into  $\rightarrow$  endothelial cells,  
 $\rightarrow$  fibroblasts &  
 $\rightarrow$  smooth ms. on injury

## Types of Capillaries:







# Lymphatic System

-1-

## Lymph Vessels:

tissue fluid (from bl. capillaries) pass to blind ended lymphatic capillaries & join → larger vessels.

\* No lymph vessels in Brain & bone marrow, Cartilage & Cornea & thymus.

### • Lymphatic capillaries:

differ from bl. capillaries in: - start e' a blind end, larger & more permeable

- Non-penetrated endoth. but wide gaps bet. endothelial cells e' no tight junctions - Interrupted b.m.

- Functions: 1. returns lymph to blood.

2. the gaps bet. endothelial cells & the interrupted b.m. help to remove large molecules as ptns, fat droplets & bact. w cannot be carried by bl. capillaries.

### • Small & Med. Sized lymph vessels:

Similar to venules but:

- Have thinner wall, larger diameter & wider lumen & more
- bicuspid valves (flow in 1 direction) → beaded appearance
- T. Media has long. & circ. smooth ms.

### • Lymph ducts:

Similar to large veins but:

- T. Media: long. & circ sm. ms + elastic fibres.

- Adventitia: have long. sm. ms + Vasa Vasora.

**Lymphangitis** = infl. of lymph vs. In skin → appear as painful red lines:

## Lymphatic tissue

= lymph follicles (nodules) + diffuse lymphocytes.

Lymphatic Organs: → 1<sup>st</sup> [central] = Bone Marrow, Thymus.

→ 2<sup>nd</sup> [peripheral] [ Lymph Node  
Spleen  
Tonsil  
MALT

mucosa associated  
lymphatic tissue



# Lymph Node

-1-

**def.:** encapsulated kidney shaped lymphatic organs along the course of lymph vessels to filter lymph from any organism.

**Site:** in groups all over the body e.g. neck, axilla, groin, thorax & abdomen

**Structure:**

## Stroma:

1. Capsule := dense c.t.  $\rightarrow$  cells [mainly fibroblasts] fibres [collagenous & elastic] . Thin  
- thickened only at the hilum due to presence of smooth muscles.  
- covered e' adipose c.t.
2. Trabeculae := c.t. septa = c.t.  $\rightarrow$  cells & fibres  
- descend from the deep surface of the capsule to divide the cortex into regular compartments. In the medulla, they branch to divide it  
" irregular " " "
3. Reticular c.t. • formed of reticular cells & fibres. In the background stains brown e' Ag. • Condensed at the follicles.

## Parenchyma:

I. Cortex: formed of:

(a) Cortical lymph follicles [nodules]:

- 1<sup>st</sup> lymph follicles:  
- rounded, oval or pyramidal = aggregations of small lymphocytes mainly B, few T- lymphocytes + antigen presenting cells + reticular cells.  
- When exposed to specific antigen, some of the lymphocytes will become activated [large lymphocytes] & collect in the centre to form pale germinal centre & change into  $\rightarrow$

- 2<sup>nd</sup> lymph follicles:  
follicles e' dark peripheral part of small lymphocytes e' dark nuclei & pale germinal centre containing large activated B-lymphocytes, lymphoblasts, plasmablasts, plasma cells, some T- lymphocytes, macrophages & reticular cells.

(b) Thymus dependant Zone = Paracortex.  
= the deep part of the cortex [bet. cortex & medulla], contains T-lymphocytes w have migrated from the thymus through post-capillary venules, lined e' s. cub. epith.



## ③ - Cortical Lymph Sinuses:

-2-

The spaces bet. cortical follicles & capsule & trabeculae subdivided into subcapsular & trabecular sinuses. lined e' endothelial cells & macrophages. Contain  $\beta$  lymphocytes, plasma cells & macrophages

## ② Medulla: formed of:

### ① Medullary Cords:

- irregular aggregations of B-lymphocytes, plasmablasts & plasma cells.
- may be continuous e' the cortical follicles.

### ② Medullary sinuses:

- spaces bet. med. cords & trabeculae. lined e' endothelial cells & macrophages.
- contain lymph received from the cortical sinuses.

## Circulation of Lymph

aff. lymph vessels enter through the outer convex border (have valves to allow lymph to move in one direction) & pour into the cortical then the medullary sinuses & drain into efferent lymph vs  $\bar{w}$  come out from the hilum.

## Blood Supply

Arteries enter from the hilum & their branches give capillaries to supply the cortex  
→ post-capillary venules → veins that leave at the hilum.

## Cells in Lymph Node

Stromal cells: Fibroblasts & reticular cells.

Parenchymal cells: •  $\beta$ -lymphocytes: in cortex & medulla.

- activated lymphocytes + plasmablasts & lymphoblasts in the germinal centre.
- plasma cells & macrophages.
- T-lymphocytes in the thymus dependent zone.
- endothelial cells lining the sinuses.

## Functions of Lymph Node

1. Filtration of lymph from any organism: by macrophages.

2. Formation of lymphocytes: in the germinal centre.

3. Immunological function:

① Humoral Immunity:  $\beta$ -lymphocyte are activated by T-helper cells → plasma blasts → plasma cells  $\bar{w}$  secrete antibodies.

② Cell Mediated Immunity: direct destruction of bacteria.  
Also T-Killer cells secrete lymphokines to destroy the antigen.



# The Spleen

- 3 -

def. Single, intra-abdominal hemolymphatic organ, along the course of blood to filter blood from any organism.

## Structure

### Stroma:

1. Capsule: formed of c.t.  $\left\{ \begin{array}{l} \text{cells: mainly fibroblasts} \\ \text{fibres: " collagenous \& elastic} \end{array} \right.$  • Thick, rich in smooth ms • covered e' peritoneum.
2. Trabeculae: " " "  $\left\{ \begin{array}{l} \text{cells -} \\ \text{fs} \end{array} \right.$  • Thick, rich in smooth ms • carry bl. v. s. n. v. • few descend from the capsule but they mainly arise from the hilum. • divide the spleen into irregular compartments.
3. Ret. c.t.: ret. cells & fibres • in the background • stained e' Ag. • condensed at white pulps.

### Parenchyma:

In fresh sections: it shows white spots on red background i.e. divided into:

#### 1. White Pulp [Malpighian Corpuscles]

Rounded or oval, scattered follicles e' an arteriole on one side = central arteriole or follicular arteriole. Formed of reticular c.t. on w. cells are arranged in 4 concentric zones around the arteriole:

(a) thymus dependent Zone = Peri-arteriolar Lymphatic Sheath [PALS]  
Contain T-lymphocytes w. ensheath the arteriole.

(b) Germinal Centre: pale area, contains activated large  $\beta$ -lymphocytes, plasmablasts, plasma cells & macrophages.

(c) Follicular Zone = Corona = dark, contains  $\beta$ -lymphocytes.

(d) Marginal Zone: at the periphery, contain T. & B-lymphocytes, plasma cells & macrophages.

#### 2. Red Pulp appears red in fresh section (large No of RBCs). formed of:

##### (a) Splenic Cords: Billroth Cords:

the areas bet. the white pulps & bl. sinusoids, contain bl. cells [RBCs, granular WBCs + lymphocytes & monocytes] + plasma cells & Macrophages & platelets

##### (b) Blood Sinusoids:

Wide irregular bl. spaces lined e' elongated fenestrated endoth. [Stave cells] e' non-continuous basement membrane for easy passage of bl. cells to blood. Macrophages appear in the wall of the sinusoid to engulf any foreign body [Littoral cells]



- 4 -

5. Blood sinusoids in red pulp: carry b/c (open or closed routes).

### 1. Open Circulation theory:

## 2. Closed Circulation theory:

### 3. Open & Closed Circulation theory:

" " " is relaxed, " " " open.

1. Filtration of blood : from any organism by macrophages.

3. Formation of bl. cells: in embryo & lymphocytes: in the germinal centre.

- Globin  $\rightarrow$  a.a.s  $\rightarrow$  blood.

5. Immunological functions : the reticular cells trap the antigen & present it to lymphocytes  $\Rightarrow$  Humoral & Cell Mediated Immunity.



| Lymph Node                                                                                                                                                                                                                                                                                                                                         | Spleen                                                                                                                                                                                                                                                 |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>No. &amp; Site</b> <ul style="list-style-type: none"> <li>multiple, small</li> <li>along the course of lymph vs.</li> </ul>                                                                                                                                                                                                                     | <ul style="list-style-type: none"> <li>single &amp; large.</li> <li>intra abdominal.</li> </ul>                                                                                                                                                        |
| <b>Functions</b> <ul style="list-style-type: none"> <li>Filter lymph</li> <li>Humoral &amp; cellular immunity</li> </ul>                                                                                                                                                                                                                           | <ul style="list-style-type: none"> <li>filter &amp; stores blood.</li> <li>Immune functions.</li> </ul>                                                                                                                                                |
| <b>Capsule:</b> thin, covered w/ fascia (fat) <ul style="list-style-type: none"> <li>smooth ms only at the hilum</li> <li>have afferent &amp; efferent lymph vs.</li> </ul>                                                                                                                                                                        | <ul style="list-style-type: none"> <li>thick, covered w/ peritoneum.</li> <li>rich in smooth ms</li> <li>No afferent lymph vessels.</li> </ul>                                                                                                         |
| <b>Trabeculae:</b> thin, descend from the capsule                                                                                                                                                                                                                                                                                                  | <ul style="list-style-type: none"> <li>thick, mainly arise from the hilum</li> </ul>                                                                                                                                                                   |
| <b>Parenchyma:</b> Cortex & Medulla <ul style="list-style-type: none"> <li><u>Cortex</u> = regular<br/>[Cortical follicles + sinuses]               <ul style="list-style-type: none"> <li>Follicles have clear germinal centre but <u>no</u> central arteriole</li> </ul> </li> <li><u>Medulla</u> → medullary cords &amp; " " sinuses</li> </ul> | <ul style="list-style-type: none"> <li>White pulp &amp; red pulp.</li> <li><u>White pulps</u> : scattered<br/>No sinuses.</li> <li>Have central arteriole.</li> <li><u>Red pulp</u> → splenic cords<br/>                    → bl. sinusoids</li> </ul> |
| <b>Cells:</b> <ul style="list-style-type: none"> <li>→ lymphocytes</li> <li>→ plasma cells</li> <li>&amp; → macrophages</li> </ul>                                                                                                                                                                                                                 | <ul style="list-style-type: none"> <li>→ RBCs, WBCs</li> <li>→ plasma cells.</li> <li>→ macrophages.</li> </ul>                                                                                                                                        |

### Clinical Notes:

Lymphadenitis: enlarged & inflamed lymph nodes draining infected area.

**Carcinoma:** spread from the 1<sup>st</sup> site through lymphatics to the regional lymph nodes w become enlarged. so they are usually removed during surgical excision of the cancer.

∴ Examination of lymph Nodes gives information about cancer spread



## The Tonsil

def.: partially capsulated lymphatic tissue, 3 sites.

### 1) Palatine Tonsils

2 oval masses of lymphatic tissue in the lat. wall of oropharynx.

Structure:

- a) lymphatic tissue → lymph follicles: e' or e'out germinal centre + diffuse lymphatic tissue = lymphocytes + plasma cells + macrophages
- b) Covered by non-keratinized st. sq. epith w̄ dips into the lymphatic tissue forming crypts in w̄ bact., lymphocytes & macrophages may accumulate.
- c) dense c.t. → incomplete capsule w̄ separate it from the adjacent structure
- d) mucous glands deep to the follicles: their ducts open on the surface & not in the base of the crypt so inflammation is common.

N.B. Salivary Corpuscles: = lymphocytes w̄ penetrate the epith. to appear in the saliva.

### 2) Lingual Tonsils:

- at the base of the tongue

- Formed of lymphatic tissue in the form of follicles & diffuse lymph tissue.
- Covered e' non-keratinized st. sq. epith w̄ dips down to form crypts.
- Mucous glands open into the base of the crypt → continuous washing, so inflammation is uncommon.

### 3) Pharyngeal Tonsil:

- lymphatic tissue (single mass) under the mucous memb. of the nasopharynx
- covered e' pseudostratified columnar ciliated epith. e' goblet cells w̄ is folded e' no crypts. Hypertrophy is called adenoids. الحمية

### Functions of Tonsils:

- protection of the respiratory & digestive systems from any invaders by production of antibodies.

### Clinical Note:

Tonsillitis: infection of the palatine tonsil → sore throat.  
repeated infection → enlarged & become focus of infection, so must be removed surgically [tonsillectomy].



# The Thymus Gland

-4-

**def.:** It is a primary lymphatic organ & also has an endocrine function.

**Site:** present behind the sternum. ↑ in size from 2nd year of life & involutes after puberty but continue to produce lymphocytes.

**Origin:** double origin: lymphocytes (mesodermal) & epith. reticular cells (endoderm).

**Structure:**

**A) Stroma:**

- **Capsule:** c.t < , thin.

- **Trabeculae:** subdivide the 2 lobes into incomplete lobules.

- **Reticular stroma:** reticular cells & no fibres in the background.

**B) Parenchyma:**

each lobule has outer dark cortex & inner pale medulla:

**1) The Cortex:**

It appears darker than the medulla as it is more populated w/ lymphocytes.

It's outer part contains lymphoblasts & the inner part contains lymphocytes (thymocytes) surrounded by epith. reticular cells + macrophages.

**2) The Medulla:**

The medullae of adjacent lobules are continuous.

They appear lighter than the cortex as they have less lymphocytes & more epith. reticular cells. They contain acidophilic structures called Hassall's Corpuscles.

**Hassall's Corpuscles:**

= central acidophilic masses of degenerated epith. reticular cells surrounded by concentric layers of epith. ret. cells in the medulla, ↑ w/ age.

**∴ The Main Cells present in the Cortex & medulla:**

**1) Epithelial reticular cells:**

**Origin:** endodermal.

**L.M.:** branched cells w/ basophilic cytoplasm & large pale oval N w/ prominent nucleolus.

**E.M.:** have secretory granules, their long processes contain tonofilaments.

Joined by desmosomes.

**Functions** ① the nursing cells for lymphocytes:

• Form sheets under the capsule, around the septa & bl. vs to isolate & protect cortical lymphocytes from any circulating antigen while they are programmed.

② secrete thymic hormones & factors to promote differentiation & proliferation of T-cells.

**2) T-lymphocytes:**

**Origin:** mesodermal.

• Stem cells in b.m. migrate to the thymus & give lymphoblasts (in the outer part of the cortex where they divide → lymphocytes w/ acquire receptors cell markers [thymic education] & selection through:

1. Eliminate non functioning T-cells w/ cannot bind MHC molecules to their receptors [80%]

Eliminate T-cells w/ bind self antigens → autoimmune dis.



- Eliminated T-cells  $\rightarrow$  apoptosis & removed by macrophages.
- 2-3% of functioning T-cells migrate to the medulla  $\rightarrow$  2<sup>nd</sup> lymph. organs in thymus dependent zones.

### 3. Macrophages:

around thymocytes to phagocytose degenerating thymocytes & any antigen escaping from the barrier.

### Blood thymic barrier:-

= the wall w separates newly formed T-lymphocytes in cortex of thymus from any circulating antigen. formed of:

1. Continuous endothelium of the capillaries.
2. thick continuous basement memb. of the capillaries.
3. perivascular c.t. containing macrophages to phagocytose any Ag that escape from the cap.
4. epith. reticular cells

### Functions:

protect immature T-lymphocyte (in cortex) from any circulating antigen. until they migrate to the medulla & enter the blood.

N.B. the medulla has no barrier.

absence of aff. lymph vessels protect it from any circulating antigen.

### Special features of the Thymus

1. It undergoes atrophy at puberty.
2. It's reticular cells are endodermal & do not form reticular fibres.
3. It has no B-lymphocytes, no plasma cells, no lymph nodules & no aff. lymph vessels.
4. Contains Hassall's corpuscles.

### Functions of the thymus:

#### 1. Proliferation & differentiation of T-Lymphocytes:

#### 2. Secretion of thymic hormones: by epith. reticular cells w stimulate maturation & activity of T-lymphocytes. The hormones are:

- a. Thymic humoral factor: stimulate mitosis of T-helper & T-suppressor cells.
- b. Thymopoietin: stim production of T-cytotoxic cells.
- c. Thymosin: " " lymphocytes.
- d. Thymulin: " function of T-lymphocytes esp T-suppressor cells.



# Macrophage System

[mononuclear phagocytic system]

Reticulo-endothelial system

(9)

**def.:** phagocytic cells all over the body for defense. Reticular cells & endothelial cells were thought to be phagocytic.

**Stain:** when a vital stain e.g. trypan blue or Indian ink is injected into an animal, macrophages engulf the dye & can be seen as granules by L.M.

**Origin:** blood monocytes.

**Histological characters:**

- have irregular surface [indentations] & receptors for Igs.
- have oval or kidney-shaped eccentric nucleus.
- prominent rER, well developed G.A, many lysosomes & residual bodies.

**Functions of phagocytic cells:**

1. phagocytosis of any bact. or debris (dead cells).
2. Cleaning of wounds, so help healing.
3. destruction of old RBCs, storage of iron & production of bile.
4. Antigen presenting cells, so have imp. role in immunity.

| Distribution:                                                                                                                                                                                                                                                                      | Site | Cell type                                                                                                                                                                                                                                           |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>• Blood.</li> <li>• Blood sinusoids of spleen &amp; b.m.</li> <li>• Blood sinusoids of Liver.</li> <li>• Brain (CNS).</li> <li>• C.T. + Stroma of:<br/>[lymph node, spleen &amp; b.m.]</li> <li>• Lung alveoli.</li> <li>• Skin.</li> </ul> |      | <ul style="list-style-type: none"> <li>- monocytes.</li> <li>- Littoral cells.</li> <li>- Von Kupffer cells.</li> <li>- Microglia.</li> <li>- Macrophages.</li> <li>- Dust cells &amp; heart failure cells.</li> <li>- Langerhans cells.</li> </ul> |

**(N.B) Antigen presenting cells [APC]:**

- derived from the b.m.
- belong to the immune system.
- they endocytose the antigens, digest them → small peptides that form complexes w/ molecules on their cell membranes & present them to T-lymphocytes.
- They include: **macrophages**, **M-cells**, **Langerhans** cells of the skin, **dendritic cells** & **epithelial reticular cells** of the thymus.



# Respiratory System

## Conducting part

- Conduct air to resp. part
- = Nose, nasopharynx, larynx, trachea, bronchi & bronchioles & terminal bronchioles.

### Functions of conducting part:

1. Conduction of inspired air:
  - presence of cartilage, collagen fibres → prevent collapse → patent airway.
  - Smooth ms. & elastic fibres give → flexibility & extensibility.
2. Conditioning of inspired air [Clean, moist & warm].
  - the mucosa is mostly ps. st. col. cil. epith & goblet cells (= respiratory epith)
  - the c.t. is rich in bl. caps. serous & mucous glands.

## The Nose

### Formed of:

#### 1. Vestibule:

lined e' hairy skin [hairs = vibrissae to trap dust]. It changes upwards into non-keratinized str. sq.

#### 2. Nasal Fossae:

- 2 chambers separated by bony nasal septum
- In each fossa 3 bony projections (conchae) extend from the lat. wall
- The sup. concha: covered e' Olfactory epith. \* while the middle & inf. conchae: are covered e' Resp. epith. \* = ps. st. col. cil. e' goblet cells.
- The conchae: ↑↑ surface area for resp. " to → condition the air cells  
→ create turbulence of air flow.
- The underlying C.t = lamina propria.  
rich in → large plexus of veins = **Swell bodies**  
→ mucous glands, WBCs, macrophages & plasma cells.

\* Inflammation & allergy → congestion of swell bodies of both fossae → limiting air flow.

#### \* Epistaxis:

- bleeding from the nose. It might start in the nose or sinuses due to injured vessels during forceful sneezing e' ↑↑ press. in the vascular nasal-septum.



Covers the sup. concia lined & ciliated mucosa.

## I. Olfactory Epith.

= modified ps. st. col. cil. epith. e' no goblet cells. Have 3 types of cells:

### a) Olfactory Neurons:

= bipolar nerve cells. the dendrites: extend to surface & end in olfactory vesicles e' basal bodies from w 6-8 non-motile cilia arise to ↑ surface area for odorous substances. the nuclei: present at a level bet. nuclei of the supporting & basal cells. the axons: pass to the underlying c.t. & form the olfactory nerve w pass through the cribriform plate of ethmoid to the brain

• Function: chemoreceptor for smell.

### b) Sustentacular (Supporting) Cells:

- tall col. cells e' wide apex & narrow base.
- have apical microvilli submerged in a fluid layer.
- have oval nuclei near the ~~the~~ surface.
- Cytoplasm contains yellow pigment → w give the yellow colour of mucosa
- joined to the olfactory cells by Junctional complexes.
- Function: supportive.

### c) Basal Cells:

↑ layer of short Δ cells e' dark rounded nuclei & basophilic cytoplasm. resting on the b.m. Function: stem cells for the other cells.

\* Stem cells have high capacity to replace olfactory cells.

So, exposure to toxic fumes → temporary loss of smell

Fracture of ethmoid bone → permanent loss of smell (damage of olfactory nerve)

## II. C.T. Corium = Lamina propria:

= dense c.t. rich in bl. vs., olfactory n. fs + Bowman's glands\*

= tubulo-alveolar serous glands: their ducts open on the surface. their secretion acts as solvent for odorous substances.

## The Respiratory Epith.

= ps. st. col. cil. e' goblet cells. Contains 5 types of cells:

1. Col. Ciliated cells: most numerous (300 cilia/cell). The apex of cells contain basal bodies & mit. → energy for ciliary beating.
2. Goblet Cells: next numerous: form & secrete mucous to trap dust & bacteria. the apex is rich in mucous granules.
3. Brush Cells: Col. cells e' apical microvilli & basal n. fs. Function: may act as receptors.
4. Basal Cells: short cells, rest on the b.m. but do not reach the surface. F.: act as stem cells for other cells.
5. Small Granule Cells: [Diffuse Neuroendocrine Cells]. Have basal granules e' dense core. Release hormones e.g. serotonin & catecholeamines w control caliber of airways & bl. vs.  
→ regulate mucous & serous secretion.



\* In Smokers: the ratio ciliated to goblet cells is reversed to Clean CO. the movement of mucous  $\downarrow \rightarrow$  congestion of small airways

|                    | Olfactory Mucosa          | Respiratory mucosa     |
|--------------------|---------------------------|------------------------|
| • Epith. thickness | - thicker                 | - thinner.             |
| • Cilia            | - few, long, non-motile   | - numerous, true cilia |
| • goblet cells     | - absent.                 | - present.             |
| • pigment          | - in sustentacular cells. | - absent.              |
| • b.m.             | - thin                    | - thick.               |
| • Bowman's gl.     | - present.                | - absent.              |

## Paranasal Sinuses

- Closed cavities in frontal, maxillary, ethmoid & sphenoid bones [around <sup>nose</sup> eye]
- lined e' resp. epith. w is thin e' few goblet cells.
- c.t. corium is thinner e' few mucous glands.

\* Immotile Cilia Syndrome :  $\rightarrow$  chronic sinusitis & bronchitis.

## Nasopharynx

- Connects nose & oropharynx. - lined w/ resp. epith = ps. strat. col. cell + goblet cells.
- c.t. core contains mucous glands + pharyngeal tonsils
- have two openings of Eustachian tube (connect to middle ear)

## The Larynx

- The Larynx
- Connects pharynx & trachea & 2 main functions:
    - production of sound
    - prevent food from entering trachea
  - Kept opened by Laryngeal Cartilages
    - Large: thyroid, cricoid & most of arytenoid = Hyaline Cartilage (may be calcified in old age)
    - Small: Epiglottis, corniculate, uniform & tip of arytenoid = Elastic Cart. (not " " " ")
  - Ligaments bind the cartilages.
  - lined & resp. epith: [ps. st. col. cil. & goblet cells] except the Vocal Cords
  - & lingual surface of epiglottis: lined & St. sq. epith.

## The Vocal Cords

- the upper pair = false (vestibular) folds:- covered e' resp. epith
  - prevent entrance of foreign bodies in larynx
- the lower pair = true cords:- covered e' non-kerat. st. sq. epith.
  - formed of elastic ligament + skeletal muscle
- the tension of vocal cords & the distance bet. them produce diff. sounds.



## Trachea (12 cm)

Its wall is formed of 4 layers:

### I. Mucosa:

1. respiratory epith: ps. str. col. cil. e' goblet cells
2. c.t. corium = lamina propria rich in bl. vs, ns & elastic fibres.
3. elastic memb = condensed elastic fs.

### II. Submucosa:

loose c.t. containing bl. vs, nerves, lymph follicles + muco-serous glands.

### III. Fibro-cartilagenous coat:

20 C-shaped plates of hyaline cartilage embedded in a dense fibrous c.t. They are completed posteriorly by: fibro. elastic memb (prevent overdistens) & smooth muscles called trachialis muscle to constrict the lumen & ↑↑ force of air flow during coughing & forced expiration.

### IV. Adventitia: loose c.t.

## Bronchial tree & lung

### 1. Extrapulmonary (1<sup>st</sup>) bronchus:

The trachea divides into 2 1<sup>st</sup> bronchi = have the same structure as trachea  
1<sup>st</sup> bronchi penetrate the hilum → divide to give →

### 2. Intrapulmonary (2<sup>nd</sup>) bronchi: e' narrower lumen. The wall is formed of:

#### a. Mucosa:

- pseudo-str. col. cil e' less goblet cells.
- c.t. corium rich in elastic fibres + lymphocytes [MALT]
- No submucosa.

#### b. Musculosa: spirally arranged smooth muscles → shortening & ↓ diameter

#### c. Adventitia: c.t. rich in elastic fs. & contains: plates of hyaline cartilage, mucoserous glands & lymph follicles in bet.

### 3. Bronchioles: < 5 mm in diameter. Formed of:

- a. Mucosa: Simple col. cil. epith. e' Clara cells, scattered neuroendocrine cells + neuroepith. bodies (chemoreceptor for O<sub>2</sub> level)
- c.t. corium.

#### Clara Cells: - Dome shaped, cilia free cells.

- cytoplasm contains basal r-ER, apical s-ER & glycogen granules.

Functions: 1. secrete surfactant like material.

2. protect epith. by glycoproteins in their granules
3. protect against emphysema by opposing protease w' destroy wall of alveoli
4. protect " inhaled toxins by enzs. in s-ER.
5. may act as stem cells for other epith. cells.



**b. Musculosa**: circular smooth muscles: control air flow.

**c. Adventitia**: c.t. e' no cart., no glands & no lymph follicles.

|                 | Extrapulm. bronchus                                                                                          | Intrapulm. bronchus                                                                              |
|-----------------|--------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------|
| Lumen           | - wider                                                                                                      | - narrower                                                                                       |
| Mucosa          | - less folded<br>- ps. st. col. cil. e' many goblet cells<br>- elastic memb. separates mucosa from submucosa | - more folded.<br>- same e' less goblet cells<br>- No elastic memb. but c.t. rich in elastic fs. |
| Submucosa       | - present                                                                                                    | - absent.                                                                                        |
| Cartilage       | - C-shaped rings of hyaline cartilage.                                                                       | - multiple plates.                                                                               |
| Sm.ms           | - bet. the ends of the cartilage                                                                             | - spirally arranged.                                                                             |
| Mucoserous gls. | - in submucosa                                                                                               | - in adventitia.                                                                                 |
| lymph follicles |                                                                                                              |                                                                                                  |

\* **Bronchitis**: inflammation of mucosa of bronchi w are congested e' swollen mucous glands.

|               | Intra-pulm. bronchus                                                   | Bronchiole                                                                                |
|---------------|------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|
| lining Epith. | Pseudo-str. col. cil. e' goblet cells                                  | S. col. cil. e' Clara Cells <span style="border: 1px solid black;">No goblet cells</span> |
| Musculosa     | spirally arranged sm.ms. (less developed)                              | - circularly arranged sm.ms. (more developed)                                             |
| Adventitia    | contains plates of cartilage<br>- mucoserous glands<br>- lymph nodules | - absent<br>- absent<br>- absent.                                                         |

\* **Bronchial asthma** = spasm of sm.ms of bronchioles → difficult expiration. Sympathomimetic drugs → bronchodilatation.

#### 4. Terminal bronchiole:

similar to big bronchiole but the epith. is s. cub. cil. e' Clara cells.

### The Respiratory Portion

the wall allows gaseous exchange.

#### 1. Respiratory bronchiole:

transition zone bet. conducting & respiratory parts.

- lined e' s. cubical e' few cilia + Clara Cells.
- c.t. rich in elastic fibres.
- thin layer of smooth ms.
- Some alveoli open directly in its wall.



- smooth ms. are present only at these openings to control airflow.

### 3. Alveolar Sacs :

a group of adjacent alveoli  $\bar{u}$  open in a common space e' no smooth ms. lined e' alv. epith.

### 4. Alveoli :

- the structural & functional unit of exchange of gases.
- Open in Resp. bronchioles, alv. ducts or alv. sacs.
- Separated by interalveolar septa & connected by alv. pores of Köhn.
- \* Pores : equalize pressure bet. alveoli & provide collateral circ. of air in bronchiolar obstruction.
- lined e' alv. epith. e' 2 types of cells :

#### Type I pneumocytes [squamous alv. cells]

- the main cells lining the alveoli 97%
- Flat cells e' flat nuclei & short microvilli
- Have little cytoplasm e' few organelles around the nucleus + pinocytic vesicles (turn over of surfactant & removal of small particles from alv. surface).

#### Functions :

- ① Form a thin layer for exchange of gases.
  - ② Connected by tight junction to prevent entrance of tissue fluid to alveoli.
- \* differentiated cells that cannot divide.

#### Type II = Great alv. cells = Secretory pneumocytes

- less numerous (3%)
- Cuboidal cells e' rounded Nuclei & short microvilli
- Abundant cytoplasm e' many mit., well developed G.A., r.ER, multilamellar bodies = (cytosomes)  $\bar{u}$  contain surfactant. (start to appear in last weeks of gestation)

- ① Secrete Surfactant  $\bar{u}$  line the alveoli
  - a.  $\bar{u}$  surface tension to prevent collapse at the end of expiration.
  - b. has bactericidal effect.
- ② Stem Cells : give rise to type I & II pneumocytes.

(N.B.) : In premature infants, surfactant is not enough  $\rightarrow$  difficult expansion of alveoli  $\bar{u}$  is called respiratory distress syndrome

### Interalveolar Septa

Septa bet. alveoli rich in  $\left\{ \begin{array}{l} \text{bl. capillaries} \\ \text{extravasated WBCs e.g. monocytes} \rightarrow \text{alv. phagocytes} \end{array} \right.$   
 the caps are supported by  $\left\{ \begin{array}{l} \text{elastic fs.} \rightarrow \text{allow expansion during inspiration} \\ \text{reticular fs.} \rightarrow \text{prevent overexpansion to protect delicate capillaries} \end{array} \right.$

### \* Emphysema :

permanent enlargement of alveoli due to destruction of elastic fibres in the interalveolar septa mainly due to cigarette smoking.



Blood Air (gas) Barrier : (0.1 → 1.5  $\mu$ m)

(7)

The barrier bet. bl. & alveolar air through w exchange of gases occurs :

formed of : 1. A layer of surfactant on alveolar epith.

2. Flat cells = type I pneumocytes (alveolar cells)

3. fused basement membs of type I pneumocytes & cap endotheli

4. endothelium of bl. capillaries.

### Alveolar Phagocytes

def : phagocytic cells (macrophages) that pass through alveolar epith. to alveoli so, they are seen bulging from interalveolar wall or inside the alveoli

Origin : monocytes escaping from bl. capillaries. Stained e' : vital stain (Trypan blue)

types : 1. Dust cells :

= alv. phagocytes engulfing dust particles.

Fate : Coughed (expelled) e' sputum through resp. passages.

2. Heart failure Cells :

the pulm. capillaries are congested e' blood, capillaries rupture & RBCs escape to alveoli. alv. phagocytes phagocytose RBCs & acquire red

Colour due to hemosiderin granules inside their cytoplasm.

Fate : coughed e' sputum 2. pass e' lymph vessels. 3. remain in interalv. septa.

### Pleura

Serous memb. formed of 2 layers : visceral L. covering the lung & parietal layer lining the thoracic wall. Both layers : lined e' s. sq. mesothelium & c.t. rich in Tol. vs, ns, lymph vs & elastic fibres. They are separated by Serous fluid → lubrication & easy movement of lung & reduce friction bet. the lung & thoracic wall during respiration.

### Foetal lung

- \* thick c.t. septa → clear lobulation
- \* Similar to a gland as the bronchial tree is similar to ducts & alveoli are similar to acini
- \* Alveoli are collapsed & lined e' s. cubical epith.
- \* Pulmonary vessels are congested e' blood.
- \* It differs from a gland in  $\left\{ \begin{array}{l} \text{bronchi \& bronchioles are folded.} \\ \text{presence of plate of cartilage around bronchi} \end{array} \right.$
- \* The whole lung sinks in H<sub>2</sub>O (medico-legal importance)



## Structural Changes in the resp. airway :

(8)

### 1] Mucosa :

- Epith : gradual ↓↓ in thickness (ps.st.col.cil → s.col.cil → s.cub.cil → s.cub → alv.epith.)
- Cilia & Goblet cells : goblet cells are lost first. but cilia gradually ↓↓ to clean mucous.
- Lamina propria : ↓↓ in thickness & ↑↑ elastic fs.

### 2] Seromucous glands : ↓↓ in No. No glands in bronchioles.

### 3] Cartilage : in trachea → C-shaped rings. in bronchi → plates w gradually ↓↓ in size. in bronchioles → No Cartilage [sm.ms prevent collapse]

### 4] Smooth ms :

- prominent in the lower part of the conducting portion.
- less " " " resp. " - absent in alv. wall.
- • In trachea: trachialis ms. bet. ends of Cart. rings.
- • In bronchi: spirally arranged.
- • In bronchioles: continuous circular sm.ms.



# Oral Cavity

21

(17)

## • Vestibule of mouth

= space bet. inner side of lips & cheeks & outer side of gums & teeth.

## • Oral Cavity: lined e' oral mucosa =

a) Epith. = st. sq. epith.

b) Lamina propria = c.t. rich in bl. vs, nerves, lymph vs & minor salivary gls.

In soft palate, floor of mouth & inner side of cheeks: the epith. is non-keratinized & connected to underlying tissue by loose c.t.

In Hard palate & gingiva (gums): the epith. is Keratinized & tightly bound to the periosteum by dense c.t.

## 1 The Lips

= Skeletal muscles (Orbicularis Oris) arranged circumoral mixed e' dense c.t.

### Outer surface (skin)

epidermis Keratinized st. sq. epith.  
c.t. dermis contains: hair follicles, sweat & sebaceous glands.

### Inner surface (oral mucosa)

epith: non-kerat. st. sq.  
c.t. rich in bl. vs., ns., lymph vs + labial gl\*  
but No sweat, seb gls or hair follicles.

\* Labial gland = tubulo-alveolar minor salivary gls. = mostly mucous acini e' occasional serous acini.

## The Red line (margin) = (Vermilion)

A transition zone bet. outer skin & inner mucous memb. = modified skin e' no hairs. It is transparent so show the red colour of underlying bl. vs. It is rich in sensory ns so highly sensitive. There is no sweat or sebaceous gls → so needs continuous wetting by saliva to prevent cracking.

## 2. The Cheeks

= skeletal ms = Buccinator

• Outer surface = skin e' subcutaneous c.t.

• Inner " " = Oral mucosa e' mucoserous salivary gls = Buccal gls in c.t.

## 3. The tongue

= skeletal ms. arranged in 3 directions at right angles <sup>longitudinal</sup> <sub>vertical & horizontal</sub> to ensure high degree of mobility for mastication, speech & swallowing

### \* the mucous memb. on dorsal surface:

- rough due to presence of lingual papillae on ant.  $\frac{2}{3}$  & lingual tonsil on post.  $\frac{1}{3}$ .
- covered e' partially Keratinized st. sq. epith e' papillated lamina propria.
- thick & firmly adherent.

### \* the mucous memb. on Ventral surface:

- smooth, thin, loosely adherent, no lingual papillae
- covered e' non-keratinized st. sq. epith.
- lingual gls are embedded in c.t. & bet. ms. of vent. surface.  
seromucous glands.



## Lingual Papillae

def.: Elevations of the oral mucosa (epith. & lamina propria) of the ant.  $\frac{2}{3}$  of the dorsum of tongue.  
4 types:

| Filiform                                                                                                                                                                                                                           | Fungiform                                                                                                                                                                                                                                             | Circumvallate                                                                                                                                                                                                                                                                                                                                                                            | Foliate papillae                                                                                                                                                                                                                                                                                                                  |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>Conical &amp; slightly curved</p> <p>ant. <math>\frac{2}{3}</math> of dorsal surface of tongue</p> <p>site</p> <p>No most numerous</p> <p>taste buds</p> <p>sp. Covered e' Kerat. character St. sq. epith whitish in colour</p> | <p>Mushroom like i.e. narrow base &amp; wide upper part</p> <p>edges &amp; tip of tongue &amp; scattered bot. Filiform</p> <p>less numerous (scattered)</p> <p>some</p> <p>Non-Kerat. epith C.t. is rich in bl. os</p> <p>↓</p> <p>red appearance</p> | <p>narrow base &amp; broad top not projecting on surface surrounded by circ. furrow (valley) sulcus</p> <p>V-shaped region in front of sulcus terminalis</p> <p>least common 6-14</p> <p>many on its sides</p> <p>presence of <u>Von Ebner's glands</u> = serous gls just under &amp; open into the grooves surrounding the papillae → continuous flow of fluids over the taste buds</p> | <p>2 or more parallel ridges &amp; furrows of c.t. covered e' non-Ker. st. sq. epith.</p> <p>On dorso lat. surface of tongue of rabbit, monkeys &amp; other animals but</p> <p>poorly developed in humans</p> <p>many</p> <p>Serous glands open by ducts to discharge their secretion into the clefts separating the papillae</p> |



## Taste buds:

- Onion shaped neuroepithelial structures. Have wide bases & narrow apices w̄ have a small opening = taste pore.
- specialized to receive taste stimuli: saltiness, sourness, sweetness & bitterness
- Sites: 1. Tongue papillae: circumvallate, fungiform & foliate papillae  
2. soft palate, 3. pharynx 4. Epiglottis.
- Formed of three types of cells:

### 1. Pale Gustatory (taste) Neuroepith. cells:

- pale elongated centrally located cells e' central nuclei
- have apical long processes many times > microvilli in diameter.
- their basal parts contain dense core vesicles containing neurotransmitters.
- " " " are surrounded by naked nerve fs. to carry taste sensat.

### 2. Dark Sustentacular (supporting) Cells:

- tall dark cells at the periphery & interior of the taste bud e' central nuclei
- have long apical microvilli projecting into the taste pore.
- Secrete glycoprotein material that surround the microvilli in the taste pore

### 3. Basal Cells:

- At the base of the taste bud
- Act as stem cells for renewal of taste cells & supporting cells.

## Glands of the tongue:

1. lingual glands: seromucous gls w̄ open on the vent. surface of the tip of tongue
2. Von Ebner's gls: Serous gl. just under & open into sulci (valley) around the circumvallate papillae.
3. Mucous & mixed gls: in dorsum of tongue.

## The Palate

### Hard Palate

- ant. part of roof of oral cavity
- covered e' Keratinized st. sq. epith + lamina propria of c.t.
- the mucosa is firmly bound to periosteum of maxilla & palatine bone by dense c.t.

### Soft palate

- post. part of roof of oral cavity
- covered e'
  - ↳ ant. oral part = oral = Non-Kerat. st. sq. mucosa
  - ↳ post. margin - continuous e' nasal cavity
  - resp. mucosa = ps. st. col. cil e' goblet cells
- has a core of skeletal muscles + mucous gls + lymph follicles.



# Oesophagus

Formed of 4 layers:

## 1. Mucosa : consists of:

a] Epithelium = non-Keratinized stratified squamous  
protect against rough food.

b] lamina propria = loose c.t. + simple tubular mucous gls = Cardiac gland

c] Muscularis mucosa <sup>[thin]</sup> = smooth muscles in 2 layers: inner circ. & outer long.

## 2. Submucosa :

- loose c.t. rich in bl. vs, lymph vessels & Meissner's plexus of nerves
- contains Oesophageal glands = compound tubulo-alveolar mucous glands
- their ducts open on the surface to protect the mucosa.

## 3. Musculosa :

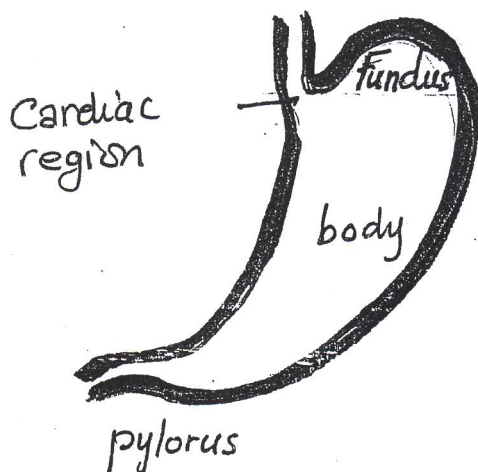
- Formed of inner circ & out. long. layers. In  $\left\{ \begin{array}{l} \text{upper } \frac{1}{3} \rightarrow \text{skeletal} \\ \text{middle } \frac{1}{3} \rightarrow \text{mixed} \\ \text{lower } \frac{1}{3} \rightarrow \text{smooth} \end{array} \right. \left\{ \begin{array}{l} \text{skeletal} \\ \text{smooth} \end{array} \right.$

## 4. Adventitia :

loose c.t. w connect the oesoph. & surroundings  
under the diaphragm it is replaced by serosa.

# Stomach

The cardiac region : the glands are lined by mucous secreting cells.  
Fundus & body : have same histological structure





## Fundus of Stomach

### 1. Mucosa :

Thick, dark & highly folded (rugae), in full stomach these long folds disappear  
formed of:

- a. Epithelium : mucous surface cells: الجدار
- b. Lamina propria : = loose c.t. containing fundic glands.
- c. muscularis mucosa : smooth muscles arranged as inner circ & out. long

### Characters of Fundic Glands

- Simple branched tubular gland
- Occupy most of the thickness of mucosa.
- perpendicular to the surface.
- highly crowded with little c.t. in between.
- Open on the surface by narrow & short pits (ducts)  
the ratio between the pit & gland 1:3 or 1:4
- Formed of isthmus, neck & body (base)
- lined by 6 types of cells: الجدار

### 2. Submucosa :

loose c.t. rich in bl. vs, lymph vs & Meissner's plexus of nerves.

### 3. Musculosa :

- Smooth muscles in 3 layers  $\left\{ \begin{array}{l} \text{inner oblique.} \\ \text{middle circular.} \\ \text{outer longitudinal.} \end{array} \right.$
- Auerbach's plexus of nerves is present bet. the circ. & long. muscle layers to regulate peristaltic movement.

### 4. Serosa : loose c.t. covered by s. sq. epithelium [mesothelium].

### Changes at the Gastro-oesophageal Junction:

1. The stratified squamous epith. of oesophagus  $\rightarrow$  simple col. at stomach

2. appearance of fundic glands.

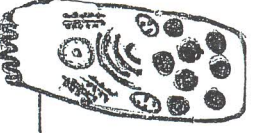
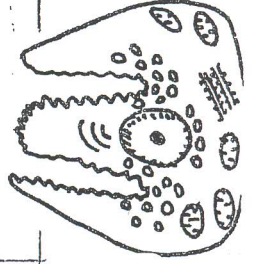
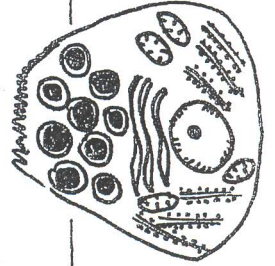
3. Oesophageal glands in submucosa disappear.

4. the musculosa becomes thicker & formed of 3 layers  $\left\{ \begin{array}{l} \text{inner oblique} \\ \text{middle circ} \\ \text{out. long.} \end{array} \right.$



# Cells Lining Mucosa of Fundus & Body

| 1. Mucous Surface cells                                                                                                                                                                                                                                   | 3. Mucous Neck Cells                                                                                                                                             | 2. Undiff. Stem Cells                                                                                                                                                                                                                                                                           | 4. Peptic = Chief = Central cells                                                                                                                                                                                                   | 5. Parietal or Oxyntic Cells                                                                                                                                                                                                                                                                                                    | 6. Entero-endocrine Argentaffin or APUD                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>- surface, pit. v</li> <li>- isthmus //</li> </ul>                                                                                                                                                                 | <ul style="list-style-type: none"> <li>- Neck</li> </ul>                                                                                                         | <ul style="list-style-type: none"> <li>- proliferative cells</li> <li>- isthmus //</li> <li>- neck (mainly)</li> </ul>                                                                                                                                                                          | <ul style="list-style-type: none"> <li>- most numerous cells</li> <li>- w. base.</li> </ul>                                                                                                                                         | <ul style="list-style-type: none"> <li>- isthmus //</li> <li>- neck //</li> <li>- base (few)</li> </ul>                                                                                                                                                                                                                         | <ul style="list-style-type: none"> <li>- base (body)</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| <ul style="list-style-type: none"> <li>- tall Col. cell e'</li> <li>- basal oval N.</li> <li>- Apex is vacuolated due to dissolved mucin (stain red e' PAS)</li> </ul>                                                                                    | <ul style="list-style-type: none"> <li>- low Col. cell e'</li> <li>- basal flat N.</li> <li>- the whole cytopl. appears vacuolated (foamy) red e' PAS</li> </ul> | <ul style="list-style-type: none"> <li>- low Col. cell e'</li> <li>- basal oval N.</li> </ul>                                                                                                                                                                                                   | <ul style="list-style-type: none"> <li>- <math>\Delta</math> cell e' basal rounded N.</li> <li>- basal basophilic cytopl.</li> <li>- apical pale zymogen granules.</li> </ul>                                                       | <ul style="list-style-type: none"> <li>- <math>\Delta</math> or rounded cell e' central rounded N.</li> <li>- base is adherent to b.m. but apex doesn't reach surface, so, called parietal.</li> <li>- C: deeply acidophilic</li> </ul>                                                                                         | <ul style="list-style-type: none"> <li>- Col. cell e' apical rounded N</li> <li>- basal granules stained e' Ag</li> <li>- so, called argentaffin cells.</li> </ul>                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| <ul style="list-style-type: none"> <li>- rER, mit., well developed G.A.</li> <li>- (supranuclear) + apical mucin granules.</li> </ul>                                                                                                                     | <ul style="list-style-type: none"> <li>- basal rER.</li> <li>- supranuclear G.A.</li> <li>- apical mucin granules.</li> </ul>                                    | <ul style="list-style-type: none"> <li>- prominent nucleoli,</li> <li>- polysomes</li> <li>- few organelles</li> </ul>                                                                                                                                                                          | <ul style="list-style-type: none"> <li>- apical short microvilli</li> <li>- apical electron dense granules + lysosomes</li> <li>- basal rER, G.A. (supranuclear)</li> <li>- Euchromatic N.e'</li> <li>- clear nucleolus.</li> </ul> | <ul style="list-style-type: none"> <li>- Intracellular canaliculi lined e' numerous microvilli</li> <li>- mit., s-ER, some rER, small GA.</li> </ul>                                                                                                                                                                            | <ul style="list-style-type: none"> <li>- N.e' prom. nucleolus.</li> <li>- many rER &amp; mit.</li> <li>- Infranuclear G.A.</li> <li>- basal dense granules.</li> <li>- few apical microvilli to monitor contents of gastric lumen.</li> </ul>                                                                                                                                                                                                                                                                                                                                                      |
| <ul style="list-style-type: none"> <li>- Secrete Neutral mucous <math>\rightarrow</math> cover surface <math>\rightarrow</math> lubrication &amp; protection from</li> <li>• autodigestion.</li> <li>• ulceration.</li> <li>by HCl &amp; enzs.</li> </ul> | <ul style="list-style-type: none"> <li>- Secrete acidic mucous to protect against HCl.</li> </ul>                                                                | <ul style="list-style-type: none"> <li>- Renewal of other cells: proliferate <math>\rightarrow</math> differentiate <math>\rightarrow</math> migrate</li> <li>Upwards <math>\rightarrow</math> surf. epith.</li> <li>downwards <math>\rightarrow</math> peptic &amp; parietal cells.</li> </ul> | <ul style="list-style-type: none"> <li>- Secrete Gastric enzymes</li> <li>• rennin</li> <li>• pepsinogen <math>\rightarrow</math> pepsin</li> <li>• lipase</li> </ul>                                                               | <ul style="list-style-type: none"> <li>- Synthesis of HCl</li> <li>Carbonic anhydrase in sER <math>\rightarrow</math> <math>H^+ + Cl^-</math> <math>\rightarrow</math> HCl in canaliculi</li> <li><math>\therefore</math> cytopl. has normal pH</li> <li>- Secrete intrinsic factor for abs. of vit. B<sub>12</sub>.</li> </ul> | <ul style="list-style-type: none"> <li>- Secrete hrs: 5 types:</li> <li>1. G-cells <math>\rightarrow</math> gastrin <math>\rightarrow</math> stim Hcl secret</li> <li>2. E.G. <math>\rightarrow</math> glucagon <math>\rightarrow</math> <math>\uparrow</math> bl. sugar (<math>\alpha</math>-cells)</li> <li>3. E-cells <math>\rightarrow</math> endorphin <math>\rightarrow</math> pain killer</li> <li>4. D. " <math>\rightarrow</math> somatostatin <math>\rightarrow</math> anti G.H.</li> <li>5. E.C. " <math>\rightarrow</math> serotonin <math>\rightarrow</math> vasoconstrict</li> </ul> |





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- | Fundus                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Pylorus                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p><b>Mucosa</b> - thick, dark &amp; highly folded.</p> <ul style="list-style-type: none"> <li>- contains <u>Fundic glands</u>.</li> <li>• crowded, occupy most of the thickness of the mucosa.</li> <li>• Simple branched tubular gl.</li> <li>• perpendicular to the surface</li> <li>• <u>pits</u>: narrow &amp; short. (<math>\frac{1}{4}</math> - <math>\frac{1}{3}</math> of gland length)</li> <li>• lined e' surface mucous, mucous neck cells, stem cells, peptic, parietal &amp; APUD cells.</li> <li>- minimal c.t. bet. the glands.</li> </ul> | <ul style="list-style-type: none"> <li>- thin, pale &amp; less folded.</li> <li>- contains <u>pyloric glands</u>.</li> <li>• less crowded, occupy <math>\frac{1}{2}</math> the thickness of mucosa.</li> <li>• Simple branched coiled tubular.</li> <li>• not <math>\perp</math> surface.</li> <li>• <u>pit</u>: wider &amp; deeper (<math>\frac{1}{2}</math> length of gland)</li> <li>• lined e' surface, mucous, stem, few APUD, occasional parietal cells. No peptic cells.</li> <li>- abundant c.t. bet. the glands.</li> </ul> |
| <p><b>Submucosa</b> : wider</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | <p>- narrower.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| <p><b>Musculosa</b> : Thinner</p> <ul style="list-style-type: none"> <li>- 3 layers <math>\rightarrow</math> inner oblique</li> <li><math>\rightarrow</math> middle circular</li> <li><math>\rightarrow</math> Out. long.</li> </ul>                                                                                                                                                                                                                                                                                                                       | <p>- Thicker</p> <ul style="list-style-type: none"> <li>- 2 layers: inner circ: thick <math>\rightarrow</math> pyloric sphincter</li> <li><math>\rightarrow</math> Out. long.</li> </ul>                                                                                                                                                                                                                                                                                                                                             |



## Changes at rectoanal Junction:

1. S.col. epith. e' goblet cells [at rectum] → st.col. at columns of Morgagni  
→ st. sq. (non-Kerat.) at anal valve → skin at anus.
2. muscularis mucosa splits at columns of Morgagni then disappear so  
c.t. core of anal canal is continuous e' submucosa of rectum.
3. the inner circ. L. of rectum is thickened → int. sphincter.
4. " Outer long " " is thinned & pass bet. int. & ext. sphincter

## The Pharynx

. It conducts air to the larynx (resp. t) & food to oesophagus (GIT)

. Formed of :

### 1 Mucosa :

- ② epith. :
- a. Nasopharynx : resp. epith. = ps. str. col. cil. e' goblet cells.
  - b. Oropharynx : oral mucosa = Non-Keratinized st. sq. epith.
  - c. laryngeal " : " " " " " " "

③ lamina propria : contains mucous glands.

④ No muscularis mucosa but dense fibrous c.t. rich in elastic fibre

2 Musculosa : inner longitudinal & out. oblique skeletal m's



## Barrett esophagus:

## Esophagus

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Metaplastic changes in the st. sq. epith of the esophagus caused by reflux of HCl to the lower end " " " (poorly protected by the esophageal glands).

## Peptic Ulcer:

## Stomach

Erosion of the mucosa of stomach or duodenum by HCl.

## Pernicious anemia]

the most common cause of vit. B<sub>12</sub> <sup>deficiency</sup> is lack of intrinsic factor.

## Causes:

1. Autoimmune disease → destruction of gastric mucosa → Achlorhydri  
2. Gastrectomy [Partial or total], chronic or recurrent peptic ulcer e' ↓↓ intrinsic factor.

3. long term use of drugs used in ttt of peptic ulcer as Histamine H<sub>2</sub>-receptor antagonist: Zantac [Ranitidine] & Tagamet [Cimetidine] → suppress both HCl & intrinsic factor.

Recently: proton-pump inhibitors e.g. Omeprazole suppress HCl but do not affect the intrinsic factor.

## Intestine

## Zollinger-Ellison-Syndrome [Gastrinomas]

Tumor of G-cells of duodenum or pancreatic islet →

↑↑ gastrin → ↑↑ HCl → gastric & duodenal ulcers.

So, patients e' severe ulcerations of stomach & intestine & not responding to ttt. should be suspected to have a tumour e' excess gastrin.

## Hemorrhoids [Piles]:

Veins in the lamina propria w become dilated, congested & protrude from the anus → painful defecation & accompanied e' fresh blood.



## Small Intestine

The surface area for absorption is augmented by:

1. 6 meters long.
2. Plicae Circularis = circular mucosal folds ↑ surface area 3 folds.
3. Intestinal Villi = ↑↑ surface area 10 folds.
4. Microvilli = " " " 20 folds.

### Structure of small Intestine (duodenum)

Formed of 4 layers:

#### I. Mucosa:

Have finger like projection [Villi] & invaginations into c.t. core [crypts]

##### • Intestinal villi

- projections of intestinal mucosa

to ↑↑ surface area for absorption

= C.T. core & central lymph. vs. Central Lacteal

Covered e' epith. e' 3 types of cells:

1. S. col. absorbing cells.

2. goblet cells

3. Argentaffin cells [entero. endocrine]

##### • Intestinal crypt [of Lieberkühn]

- invagination from surface

= simple tubular glands surrounded by c.t.

lined e' 6 types of cells:

1. simple col. absorbing cells.

2. goblet cells.

3. Entero-endocrine cells.

4. undifferentiated col. (stem) cells

5. Paneth cells 6. M. cells.

a. Epith = Cells lining the intestinal Mucosa: look the table

b. C.T. Corium = Lamina propria:

loose c.t. form the core of villi & surround the crypts, rich in bl. vs, nerves & lymph vessels = central lacteal. + WBCs + macrophages + plasma cells

In the ileum there are lymph follicles called Peyer's patches.

c. Muscularis mucosa: thin muscle: inner circular & outer longitudinal ls.

#### II Submucosa:

loose c.t. rich in bl. vs, lymph vessels & Meissner's plexus of nerves.

- In duodenum: contains Brunner's glands = compound tubulo-alveolar mucous glands in submucosa of 1st part of duodenum, open by long ducts in base of crypts.

- In Ileum: contains Peyer's patches: lymph follicles at the antimesenteric side. of submucosa, pierce the muscularis mucosa & appear in muc. (villi over them either short or absent)

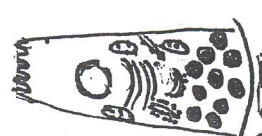
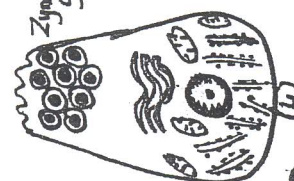
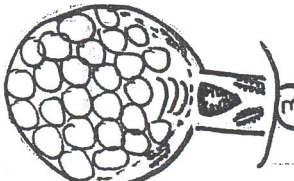
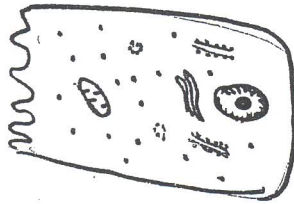
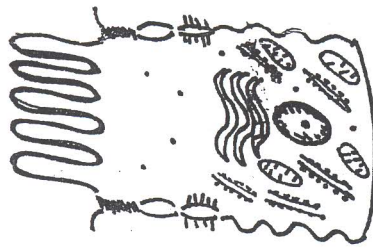
#### III. Musculosa:

Smooth muscles arranged as Inner circ. & outer long. layers separated by Auerbach's plexus of nerves.

IV. Serosa: loose areolar c.t. covered e' s. sq. mesothelium.



# Cells lining Mucosa of Small Intestine



## Col. abs. Cell [Enterocyte]

- Villi & crypts
- tall col. cell e' basal oval N. v apical acidophilic striated border.
- Apical microvilli w' surface area for absorption
- Cell coat (glycocalyx) rich in enzs e.g. sucrase, isomaltase & alk. phosphatase.
- The lat. borders show interdigitations & junctional complexes: Zonula occludens, adherens & desmosomes.
- Cytopl: rich in mit., G.A., r-ER & few free ribosomes

## Undifferentiated Col. cells

- crypts.
- short col. cell basal oval N. many cells show mitosis
- Smooth lat. wall e' no interdigitations
- few rER & mit
- small G.A.
- many free ribosomes & polysomes.

## Goblet Cells

- Villi & crypts (bet. enterocytes)
- basal cylindrical part e' dark N
- apical clear flask-shaped part.
- Apical pale mucous containing granules
- some mit.
- supranuclear G.A.
- abundant r-ER in the basal & lat. part.

## Paneth Cells

- base of crypt of a villus
- Δ cell e' basal rounded N.
- basal basophilic cytoplasmic acidophilic
- Zymogen grs.
- basal // cisternae of rER, mit.
- supranuclear G.A.
- apical electron dense zymogen granules + lysosomes

## M cells

- microfold cells
- crypts over Peyer's patches
- modified squamous cells.
- Function: Antigen presenting cells: phagocytose & transport antigens in intestinal lumen to underlying lymphocytes

## Argentaffin cells

- Entero-endocrine "APUD" cells.
- Crypt (base) + Villi (few 1%)
- Col. cell e' apical round N. basal granules stained E.M.
- Ag. so called argentaffin mit., rER, polysomes
- Infranuclear G.A.
- basal dense grs.
- apical microvilli to monitor intest. contents.

## F. → Intestinal hrs.

1. G. cells → gastrin
2. E.G. (α-cells) → enteroglucagon
3. E. cells → endorphin (pain killer)
4. D. cells → Somatostatin
5. E.C. cells → Serotonin
6. S. cells → secretin
7. Mo. cells → motilin
8. N. cells → neurotensin
9. I. cells → Cholecystokinin - Pancreozymin
10. K. cells → Gastric inhibitory peptide

- functions
1. Complete digestion of polys & CHO by enzs in glycocalyx
  2. Absorption of glucose, a.a.s, F.A & mono glycerides

- Unicellular Gl. secrete mucous at intervals for protection & lubrication
- ↑ No from duod. to ileum ??

- Secrete:
- Intestinal enzs & lysozyme (anti-bact)



# Large Intestine

**Formed of:** Cecum, colon [ascending, transverse, descending & sigmoid] & rectum. The appendix projects from cecum. Large intest opens to exterior by the anal canal.

## Cecum & Colon

Histologically, have the same structure: Formed of:

### I. Mucosa:

- No villi but only deep & wide crypts:

#### (a) Epith.:

- the surface is covered e' col. absorbing cells (e' striated border) + goblet cells  
- Crypts are lined e' col. absorbing cells, numerous goblet cells, basal stem cells, few argentaffin cells but **No Paneth cells**.

(b) C. t. corium = lamina propria = c. t. containing solitary lymph follicles

(b) Muscularis mucosa: inner circular layer & out. long. l. of smooth muscle

### II. Submucosa:

C. t. rich in bl. vs, ns, lymph vs but no glands.

### III. Musculosa:

The inner circular layer is continuous while the out. long. layer is not but arranged in 3 bundles called **Tenia Coli**.

### IV. Serosa:

C. t. rich in fat cells forming projections covered e' peritoneum (s. sq.) called **appendices epiploicae**

## Vermiform Appendix (2-8 cm)

project from the cecum. has narrow lumen formed of:

I. Mucosa: No villi only few & short crypts:

(a) Epith.: Col. absorbing, goblet cells, stem cells, argentaffin + M-cell

(b) lamina propria: c. t. corium e' lymph follicles w extend to submucosa

(c) No muscularis mucosa: so mucosa is continuous e' submucosa

II. Musculosa: very thin: inner circular & out. long (continuous i.e. **No Tenia Coli**)

III. Serosa: c. t. covered e' s. sq. mesothelium (no appendices)

## Rectum (12 cm)

Similar to Colon but fewer & deeper crypts e' more goblet cells  
No tenia coli. No peritoneum. So serosa is replaced by adventitia



### Differences bet. the 3 segments of small Intestine

|              | Duodenum                                    | Jejunum                                              | Ileum                                                   |
|--------------|---------------------------------------------|------------------------------------------------------|---------------------------------------------------------|
| Length       | - 25 cm                                     | - 2.5 meters                                         | - 3.5 meters.                                           |
| Villi        | - long & broad<br>(leaf-like)<br>- numerous | - shorter &<br>(tongue-shaped)<br>- less numerous    | - short & slender<br>(finger-like)<br>- least numerous. |
| Goblet cells | - few                                       | - more                                               | - most numerous.                                        |
| Submucosa    | - Contains Brunner's<br>glands              | - Neither Brunner's<br>glands nor Peyer's<br>patches | - Peyer's patches.                                      |

### Changes at pyloro-duodenal Junction:

1. appearance of villi in the duodenum.
2. Columnar cells acquire brush border (microvilli)
3. appearance of goblet cells.
4. pyloric glands are replaced by intestinal crypts
5. appearance of Brunner's glands in submucosa of duodenum
6. musculosa become thinner in duodenum.



| Small Intestine                                                                | Large Intestine                                                       |
|--------------------------------------------------------------------------------|-----------------------------------------------------------------------|
| length - About 6 meters                                                        | - 180 cm                                                              |
| diameter - small                                                               | - larger                                                              |
| segments - duodenum, jejunum, & ileum                                          | - Cecum, colon, rectum                                                |
| <u>Mucosa</u> - villi & crypts                                                 | - No villi, only crypts (deeper)                                      |
| cells col. absorbing, goblet, stem, M-cells & paneth cells, APU: D cells       | - more goblet cells                                                   |
| c.t. contains WBCs, lymphocytes & plasma cells bet. crypts                     | - No paneth cells.                                                    |
| <u>Submucosa</u> : have Brunner's gls in duodenum. & Peyer's patches in ileum. | - contains solitary lymph follicles + diffuse lymphocytes bet. crypts |
| <u>Musculosa</u> Inn. circ. & Out. long. } continuous                          | - Neither Brunner's gls, nor Peyer's patches.                         |
| <u>Serosa</u> : = c.t. & s.sq. mesothelium.                                    | - Out. long. is in 3 bundles → Tenia Coli.                            |
|                                                                                | - Accumulation of fat cells → appendices epiploicae.                  |

## Anal Canal [3-4 cm]

- the few crypts start to disappear
- **Mucosa**: have long. folds = Columns of Morgagni w join at their ends → anal valves separated by anal sinuses.
- lined e' simple col. (2cm) → st. col. at Columns of Morgagni → non-kerat. st.sq. at anal valve → skin at anus. e' sebaceous & sweat glands + perianal apocrine sweat glands.
- the lamina propria contains plexus of veins that may show varicosity, become distended e' blood & dilated & bulge from the anus → piles [hemorrhoids]
- Muscularis mucosa splits then disappear.
- **Musculosa**: Inner circular & Out. long.
  - the inner circular is thickened → internal sphincter
  - the out. long. is thinned & pass bet. the int. & ext. sphincters
  - the levator ani [skeletal ms of pelvis] form ext. sphincter.



# Salivary glands

(1)

Major  $\Rightarrow$  90% of vol. of saliva

- Compound tubulo-alveolar
- paired 2 parotid, 2 submandibular, 2 sublingual

Functions of saliva p. 42

Minor 10%

- branched tubulo-alv.
- scattered in oral mucosa of lip, tongue, cheeks, palate, tonsil  
labial lingual buccal palatine, von Ebner's

## Parotid Gland

def.: The largest salivary gland, exocrine, comp. tubulo-alveolar, purely serous gland in front of both ears. Formed of:

### • Stroma:

a. Capsule := c.t. cells (mainly fibroblasts) & fibres (collagenous & elastic) thick, rich in fat cells. covered by fascia & skin.

b. Trabeculae := c.t. cells & fibres thick, rich in fat cells. descend from capsule to divide the gland into lobes & lobules. carry bl. vs. nerves & ducts.

c. Reticular c.t. := ret. cells & fibres in the background. stained w/ Ag.

### • Parenchyma:

Formed of Serous acini & duct system.

#### Serous acini:

- Have small diameter & narrow lumen, lined by serous cells.
- Serous cells are pyramidal cells & central rounded nuclei.
- Have non-clear cell boundaries & joined by junctional complexes.
- Cytoplasm is deeply basophilic rich in mit, r-ER, well developed G.A. & apical zymogen granules.
- Secrete serous fluid rich in amylase for hydrolysis of carbohydrates.
- The acini are surrounded by Myoepithelial cells = Basket cells.
- Branched stellate cells that surround the acini & ducts. present bet. the basal part of the cells & the basement memb. rich in actin & myosin. their contraction discharge the secretion to the ducts. & prevent distention of acini (11 intraluminal press) during secretion.

#### Duct System:

##### 1. Intercalated ducts:

- the 1<sup>st</sup> ducts w/ arise from the acini - lined by s. cubical epith. join to form

##### 2. Intra-lobular [striated] duct:

- Inside the lobules. lined by s. cuboidal cells & central rounded nuclei
- Cytoplasm is acidophilic & basal acidophilic striations.



elongated mit. - have secretory function & drain into →

### 3. Inter-lobular duct [excretory]:

In the septa bet. the lobules. lined e' s.col. epith. join to form →

### 4. Inter-lobar duct:

In the septa bet. the lobes, lined e' pseudo-st.col. " " " " →

### 5. The main duct [Stensen's duct]

lined e' stratified col. epith. w changes into str. squamous at its opening in the mouth cavity.

(N.B) The c.t. stroma contains many lymphocytes & plasma cells w secrete Ig A that together e' secretions produced by serous acini intercalated & striated ducts ⇒ Ig A-secretory complex (resistant to digestion) w defend against infection by pathogens in the oral cavity.

### Types of acini

| ① Serous acinus                                                                                                                                                                                                                                                        | ② Mucous Acinus                                                                                                                                                                            |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <p>diameter - small</p> <p>lumen - narrow</p> <p>Cells - pyramidal cells e' non-clear boundaries</p> <p>- central rounded nucleus</p> <p>- deeply basophilic cytoplasm e' apical zymogen granules</p> <p>Function - secrete serous fluid</p> <p>Basket cells - few</p> | <p>- larger</p> <p>- wide</p> <p>- cuboidal cells e' clear boundaries</p> <p>- basal &amp; flat nucleus</p> <p>- pale vacuolated (dissolved mucin)</p> <p>- mucous.</p> <p>- numerous.</p> |

### ③ Mucoserous acini:

a mucous acinus having on one side a crescent of basophilic serous cells = Crescent of Gianuzzi or Serous demilunes.

Function: secrete mucoserous secretion.



Major Salivary Glands  
Exocrine, compound tubulo-alveolar glands, secrete 90% of total vol. of saliva. They include:

|                    | Parotid (largest)                                                                                                                                                                                                                                                                                                                  | Submandibular                                                                                                                                                                                                                                                                                                    | Sublingual (smallest)                                                                                                                                                                                                                                                     |
|--------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Site</b>        | - in front of both ears                                                                                                                                                                                                                                                                                                            | - innerside of the mandible                                                                                                                                                                                                                                                                                      | - under mucosa of floor of mouth.                                                                                                                                                                                                                                         |
| <b>Capsule</b>     | - Very thick, rich in fat cells                                                                                                                                                                                                                                                                                                    | - thick                                                                                                                                                                                                                                                                                                          | - thin                                                                                                                                                                                                                                                                    |
| <b>Trabeculae</b>  | - thick, rich in fat cells                                                                                                                                                                                                                                                                                                         | - abundant trabeculae                                                                                                                                                                                                                                                                                            | - thick trabeculae                                                                                                                                                                                                                                                        |
| <b>Parenchyma</b>  | - divide the gl. into lobes & lobules                                                                                                                                                                                                                                                                                              | - divide -----                                                                                                                                                                                                                                                                                                   | - divide -----                                                                                                                                                                                                                                                            |
| <b>Acini</b>       | - carry b.l.v.s, ns, lymphus, ducts                                                                                                                                                                                                                                                                                                | - carry -----                                                                                                                                                                                                                                                                                                    | - carry -----                                                                                                                                                                                                                                                             |
| <b>Duct system</b> | <p><b>Serous:</b></p> <ul style="list-style-type: none"> <li>- purely serous</li> <li>- contain zymogen w contain amylase for hydrolysis of CHO</li> </ul> <p>similar to that of large salivary glands</p> <p><u>the main duct = Stensen's d.</u></p> <p>opens in innerside of cheek opposite 2<sup>nd</sup> upper molar tooth</p> | <p><b>Seromucous:</b></p> <ul style="list-style-type: none"> <li>• In humans, 90% serous</li> <li>10% mucous + mucoserous</li> <li>(N.B.) in dog mostly mucous</li> <li>- zymogen contain <u>lysozyme</u> kill bact.</li> </ul> <p>- same</p> <p><b>Wharton's duct</b></p> <p>opens on floor of mouth cavity</p> | <p><b>mucoserous:</b></p> <ul style="list-style-type: none"> <li>- mucous acini predominate</li> <li>- mucoserous acini but</li> <li>No. pure serous acini</li> </ul> <p>- same</p> <p>- either joins submandibular duct or open separately on floor of mouth cavity.</p> |



# Pancreas

- 4 -

def.: A mixed gl. → Exocrine part = Comp. tubulo-alveolar, serous → p. juice.  
→ Endocrine " = Islet of Langerhans → p. hormones.

Formed of:

## Stroma:

1. Capsule: c.t. cells ( ) & Fibres ( ). Thin, covered e' peritoneum
2. Trabeculae: c.t. cells ( ) . Thin, delicate, descend from capsule to divide the gl. into indistinct lobes & lobules.
3. Reticular c.t.: reticular cells & fibres. In the background. • stained e' Ag.

## Parenchyma:

### Exocrine part:

#### 1] Acini:

L.M. Have small diameter & narrow lumen.

- lined e' pyramidal cells e' non-clear boundaries.
- have basal rounded pale nuclei e' prominent nucleoli
- have basal basophilic cytopl. & apical acidophilic zymogen granules.

#### Centro-acinose Cells:

Flat cells lining the lumen of acini. They represent the invaginated or telescoped part of the intercalated duct.

E.M. - the cell membs. are joined by junctional complexes.

- basal basophilia due to many cisternae of basal r-ER.
- Supranuclear well developed G.A. - many mit.
- Apical electron-dense memb. bound zymogen granules.

#### 2] Duct System:

• Intercalated duct: narrow, lined e' s. squamous epith. they invaginate into the lumen of the acinus → centro-acinar cells.

• Intra. lobular duct: absent.

• Inter. lobular " : lined e' s. cubical epith.

• Inter. lobar " : " s. col. "

• Main pancreatic " : " s. col. + goblet cells & entero-endocrine.

(N.B) The exocrine secretion is controlled by 2 hrs. secreted by enteroendoc cells of G.I.T.

Cholecystikinin, pancreazimin: stimulate acinar cells to produce and secrete



## Biliary tract [Passages]

### (1) Bile Canaliculi:

- receive bile secreted by the liver cells.
- limited by the cell memb. of hepatocytes in the 2 rows.
- short microvilli project from the liver cells into the canaliculi.
- bile flows from the centre of the lobule to the periphery i.e. opposite the direction of blood. They empty in →

### (2) Canal of Hering [ductule]:

- lined e' s. cubical epith. receives bile from canaliculi & drain into:

### (3) Inter-lobular bile duct:

- In the portal canal, lined e' s. cubical. Fuse to form →

### (4) Rt. & Left hepatic ducts:

- the intrahepatic part is lined e' s. cubical epith.
- " extra " " " " " s. columnar " . They fuse to form →

### (5) Common Hepatic duct:

- lined e' s. col. epith surrounded by c.t. & smooth ms.
- Joins the cystic duct to form the common bile duct.

### (6) Cystic duct:

arise from the gall bladder, lined e' s. col. epith. surrounded by c.t. & sm. ms.

### (7) Common bile duct: lined " " " " " " " " " "

the c.t. under the epith. contains mucous glands  
the muscle is thickened near the duod. to form **sphincter of Oddi** to regulate bile flow.

## The Gall Bladder

def A pear shaped hollow organ attached to the lower surface of liver.

Function: stores, concentrates bile & adds mucous. Formed of:

### 1. Mucosa: (highly folded)

- a. s. col. epith: provided e' microvilli (absorb  $H_2O$ ) & can secrete mucous.
  - b. lamina propria: rich in bl. vs & tubuloalveolar mucous gls.
- No muscularis mucosa, so no submucosa.

### 2. Musculosa: i

irregular smooth ms e' elastic & collagenous fs in bet.

### 3. Serosa: covered e' peritoneum (except hepatic surface)



## Endocrine part:

- pale areas among the dark acini.
- about 1 million but mainly in the tail.
- Non-capsulated but supported by reticular c.t.
- Formed of masses or branching cords of cells separated by  $\rightarrow$  Penetrated capillaries or bl. sinusoids. Contain 7 types of cells:

| ①. Beta $\beta$ - cells                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | ②. Alpha $\alpha$ - cells                                                                                                                                                                                                                                                                                                                                |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>• more numerous 70%.</li> <li>• smaller diameter (10-15 <math>\mu</math>m).</li> <li>• centrally located.</li> <li>• Basophilic grs. (alcohol soluble)</li> <li>• E.M. rich in mit., well developed G.A., rER., memb. bound electron dense grs.</li> <li>• Funct<sup>n</sup>: secrete insulin <math>\bar{w}</math> <ul style="list-style-type: none"> <li><math>\hookrightarrow</math> lowers bl. sugar.</li> <li><math>\hookrightarrow</math> help glycogenesis.</li> </ul> </li> </ul> | <ul style="list-style-type: none"> <li>- less numerous 15%.</li> <li>- larger (15-25 <math>\mu</math>m).</li> <li>- peripherally situated.</li> <li>- Acidophilic grs. (H<sub>2</sub>O soluble).</li> <li>- secrete glucagon <math>\bar{w}</math> <ul style="list-style-type: none"> <li><math>\uparrow\uparrow</math> bl. sugar.</li> </ul> </li> </ul> |

### ③. Delta ( $\delta$ ) cells:

- 10% of the cells. peripherally situated.
- contain secretory granules  $\bar{w}$  stain e' Ag.
- Funct<sup>n</sup>: secrete somatostatin = anti growth hr. control release of insulin & glucagon

### ④. C. cells:

- very few (3%), have few organelles, few granules.
- F: unknown: may be immature or degranulated cells.

### ⑤. F (P.P.) cells:

- very few, few organelles, few granules.
- F: secrete pancreatic polypeptide  $\bar{w}$  reduces pancreatic secretion.

### ⑥. G. cells: secrete gastrin.

### ⑦. Ganglion Cells: sympathetic n. cells $\rightarrow$ autonomic nervous control of islet secret



| Parotid                                                                                 | Pancreas                                                                                                  |
|-----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------|
| Exocrine (pair)<br>in front of both ears                                                | - mixed (single).<br>- in concavity of duod.                                                              |
| <u>Capsule</u> : thick, rich in fat<br>covered e' fascia then skin                      | - thin & delicate, no fat.<br>- covered e' peritoneum.                                                    |
| <u>trabeculae</u> : thick → distinct lobulation                                         | - thin → indistinct lobulation.                                                                           |
| <u>Acini</u> have basophilic cytoplasm &<br>central rounded nuclei                      | - <del>Basal</del> basophilic cytopl. & apical<br>acidophilic zymogen granules +<br>basal rounded nuclei. |
| <u>Basket</u> - present.<br><u>cells</u>                                                | - absent.                                                                                                 |
| <u>Centracinose</u> : absent.<br><u>cells</u>                                           | - present.                                                                                                |
| <u>Intercalated</u> : not invaginated.<br><u>duct</u>                                   | - invaginated.                                                                                            |
| <u>Intralobular</u> present.                                                            | - absent.                                                                                                 |
| <u>Main duct</u> : lined e' st. col. then<br>st. sq. at it's opening in<br>mouth cavity | - lined e' s. col. + goblet cells<br>+ enters endocrine cells                                             |
| <u>Islets of Langerhans</u> : absent                                                    | - present.                                                                                                |



# Liver

def: The largest metabolic gland. Mixed gland → Exocrine = comp. tubular → bile  
→ endocrine → glucose, plasma-proteins & lipoproteins → blood.

## Functions:

1. Form bile
2. Form plasma proteins, a.a.s, uric A & urea.
3. storage of glycogen, vitamins [KDA & B] & minerals [Fe & Cu].
4. detoxification of drugs & hormones.
5. destruction of old RBCs & dead cells by macrophages.
6. Metabolism of CHO, lipids & proteins.
7. Secrete Ig A & M.

## Structure:

### I. Stroma:

#### A. Capsule [Glisson's]:

- C.T. cells  
- fibres

thin, partially covered e' peritoneum.

#### B. Trabeculae:

C.T. cells

& fibres, delicate in human → non-clear lobulation but in pig & in man (in case of cirrhosis) it is very thick. It is condensed at the corners of the lobules surrounding bl. vs & bile ducts.

#### C. Reticular C.T.:

• reticular cells & fibres • in the background • stained e' Ag.

### II Parenchyma:

Both exocrine & endocrine functions are carried by the structural unit [Hepatocyte] which are arranged in ① Classic hepatic lobule ② Portal lobule ③ Liver sinusoid

#### 1. Classic Hepatic lobule

def Hexagonal mass of liver cells draining their venous blood into a central vein. demarcated by thin trabeculae which are thickened at the corners →

#### Portal tracts or Canals:

condensed C.T. at the corners bet. hepatic lobules. It contains:

- ① A branch of portal vein: the widest.
- ② " " " hepatic artery: rounded, narrow lumen
- ③ A bile duct (Cub. epith)
- ④ A lymph vessel.

Liver cells are arranged in the form of cords [or plates] radiating from the central vein. The cords are separated by bl. sinusoids. Each cord is formed of 2 rows enclosing a bile canaliculus. The fenestrated endoth. of bl. sinusoids is separated from hepatocytes by space of Disse.



# Liver Cell [Hepatocyte]

- 2-

L.M. large polyhedral cell e' central 1 or 2 nuclei: pale, vesicular e' prominent 1 or 2 nucleoli & acidophilic (mit. & SER) & vacuolated cytoplasm (dissolved) glycogen. Glycogen (stained e' PAS or Best's Carmine).

## E.M. [1] Cell Membrane:

- a. surface facing bl. sinusoid shows long Microvilli for transfer of materials bet. liver cell & bl. sinusoid
- b. " " bile canaliculus " short " "
- c. " " adjacent hepatocyte " junctional complexes.

## [2] Cytoplasm: contains all organelles & inclusions:

a. Mitochondria: numerous 1000-2000/cell → energy production.

b. free ribosomes → ptn. to build the cell

c. r-ER → form plasma proteins.

d. s-ER: abundant → synthesis of cholesterol, phospholipids.  
→ detoxification of drugs & hrs.  
→ break down & storage of glycogen.

e. G.A. well developed: → secretion  
→ form lysosomes.  
→ turnover of cell memb.

f. lysosomes: numerous → destroy old components or organelles.  
→ eliminate waste products.

g. Microbodies [peroxisomes]: v. numerous for metabolism of  $H_2O_2$   
" " etc.  
→ degradation of lipids.

Inclusions: a. fat droplets.

b. glycogen = electron dense granules.

## Bl. Sinusoids:

Irregular bl. spaces radially arranged bet. the hepatic plates (demonstrated when injected e' gelatin Carmine). Lined e' 2 types of cells:

(1) fenestrated endothelial cells.

(2) von Kupffer cells:

- branched phagocytic cells e' pseudopodia lining liver sinusoids.
- Origin: bl. monocytes. - sp. stain: vital stain (trypan blue)
- Cytoplasm is vacuolated rich in lysosomes & phagocytic vesicles

### Functions:

1. Clean bl. passing from portal vein to central vein from foreign material → prevent obstruction of bl. sinusoids.
2. destruction of old RBCs & form bile pigments.
3. phagocytose any bact. or microorganism coming from the intestine.



Space of Disse [Perisinusoidal space]

- It is the space bet. hepatocytes & bl. sinusoids.

- Contains:

- long microvilli projecting from hepatocyte (↑ surface area bet. hepatocytes & plasma)
- plasma containing nutrients.
- reticular fibres [support the wall of the sinusoid].
- Ito cells: branching fat storing cells store vit. A in fat droplets as retinyl ester.

## 2. Portal lobule

def. a triangular mass of liver cells including parts of 3 adjacent hepatic lobules. It drains its bile into the bile duct in the portal canal in the centre of the lobule. Has 3 central veins at the apices of the lobule.

## 3. Liver Acinus

def. a diamond shaped mass of liver cells including parts of 2 ady. hepatic lobules. It has a central vascular core = branch of a hepatic art. & branch of a portal vein that arise at right angle from the portal canal.

- It is divided into 3 zones:

- Zone I: close to the vascular core rich in bl. supply [1<sup>st</sup> to receive glucose +  $O_2$ ]
- Zone II: intermediate zone, less bl. supply than Zone I.
- Zone III: At the periphery of acinus farthest from vascular core & nearest to central vein. poor in bl. supply [least  $O_2$  & glucose].

This explains why in certain diseases some cells are more affected than the others.

## Bl. Supply of liver

75% of the bl. supply comes from the portal vein [nutrient rich but  $O_2$  poor] while 25% " " " hepatic art [ $O_2$  rich]. They pour from periphery to centre of the lobule (in bl. sinusoids).

## The Gall bladder

Pear shaped organ attached to the lower surface of the liver.

Function: stores & concentrates bile & adds mucus. Formed cfa

Structure:

1. Mucosa: highly folded (no villi & no crypts).

= simple col. epith. → e' apical microvilli (to absorb  $H_2O$ )

↳ secrete mucus

• lamina propria = c.t. rich in bl. vs & tubuloalveolar mucous gls

• no muscularis mucosa. no submucosa.

2. Musculosa:

irregular smooth ms + collagenous & elastic fibres.

3. Serosa: except at the hepatic surface.



# ENDOCRINE SYSTEM

1. Glands, e.g. pituitary, suprarenal, thyroid, parathyroid glands and pineal body.

2. Masses of cells, e.g. endocrine part of pancreas, testis, ovary, thymus ....

3. Cells scattered all over the body, e.g. APUD cells.

\*They have no ducts but fenestrated capillaries or blood sinusoids to carry hormones directly to the blood.

## Pituitary Gland (Hypophysis Cerebri)

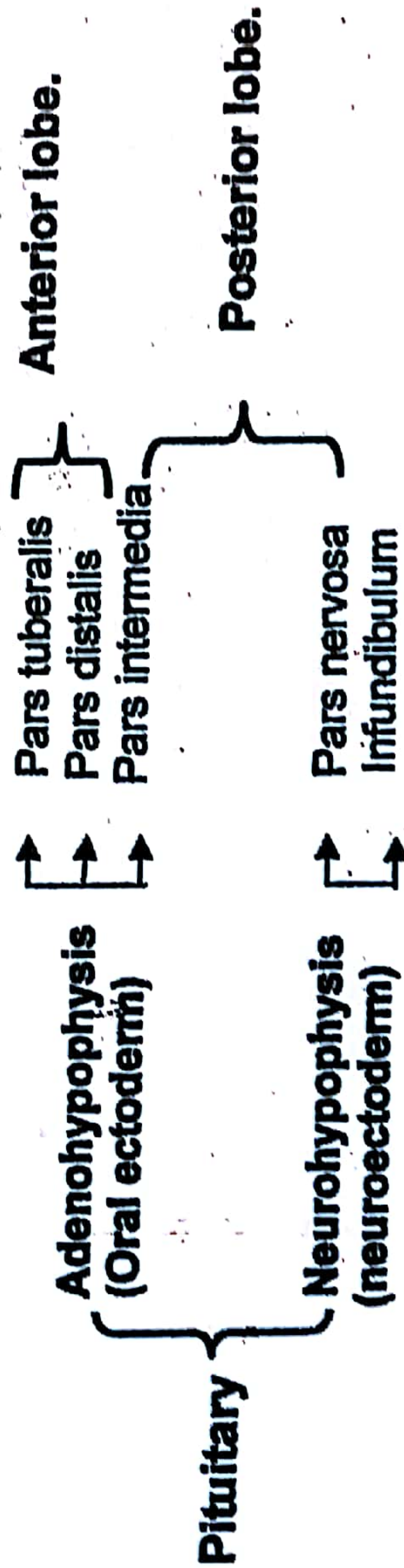
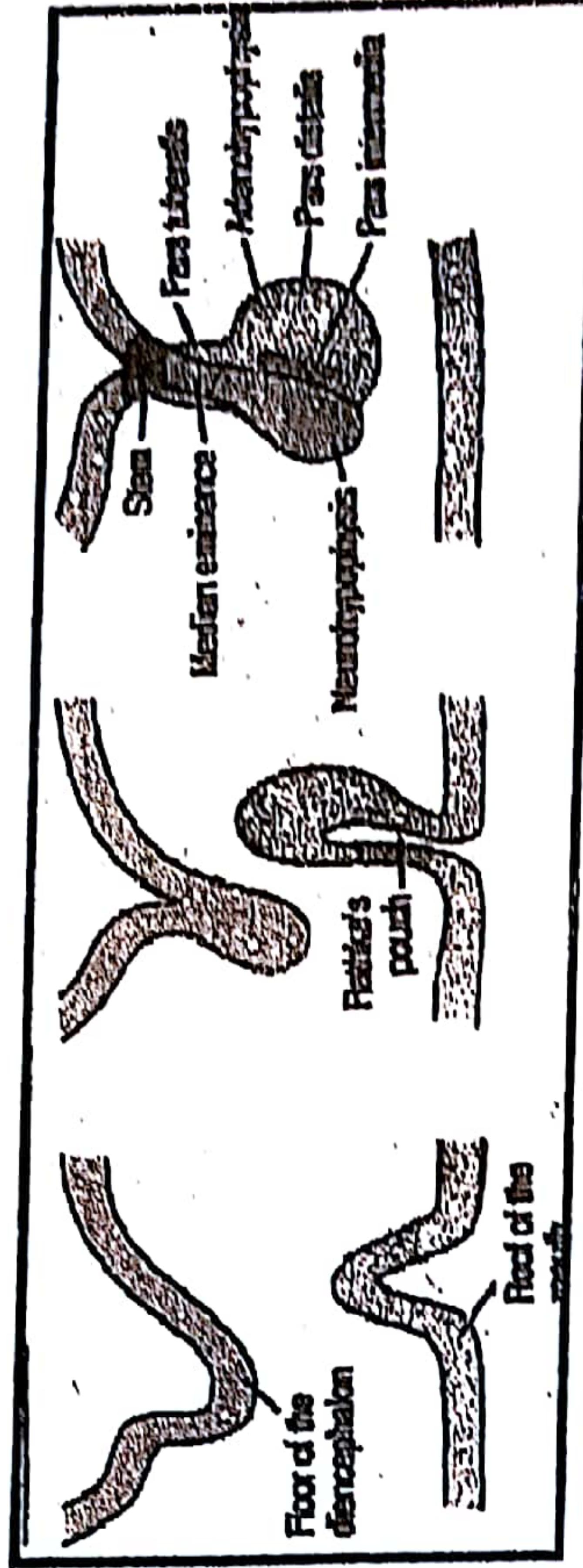
- \* Present in the base of the skull in (sella turcica).
- \* Connected to the hypothalamus by infundibular stalk.

Formed of:

**Adenohypophysis:** develops from oral- ectoderm as upward growth from roof of oral cavity forming Rathke's pouch.

**Neurohypophysis:** develops from neuroectoderm as downward growth from floor of diencephalon.

Both components unite to form pituitary gland.





# Adenohypophysis

## 1. Pars Distalis

- \*covered with a thin C.T. capsule & supported by reticular C.T.
  - \* Formed of cells arranged in groups or branching cords separated by fenestrated capillaries.
  - \*cells are classified into 2 groups: chromophobes & chromophils.
- A. Chromophobes (52%):**

  - Small cells with pale cytoplasm (has mild affinity for stains).
  - Some are granular & may secrete hormones.
  - Some are non-granular & are considered as stem (undifferentiated) cells or exhausted chromophils.

**B. Chromophils (48%):**

  - Have affinity for stains.
  - Classified into: acidophils and basophils.
- I. Acidophils(37%)**

  - Medium sized cells between chromophobes and basophils.
  - **Two types:**
  - (a) somatotrophs &
  - (b) mammotrophs.

**2. Basophils (11%)**

  - The largest cells.
  - Cytoplasm has basophilic granules
  - **Three types:**
  - (a) thyrotrophs.
  - (b) corticotrophs.
  - (c) gonadotrophs.

| Acidophils of the pars distalis |                                                                                                                                                                                                                             |                                                          | Basophils of pars distalis.                                                                                    |                                                                                       |                                                                                                                                                                                           |
|---------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Cell type                       | (a) Somatotrophs                                                                                                                                                                                                            | (b) Mammotrophs                                          | (a) Thyrotrophs                                                                                                | (b) Corticotrophs                                                                     | (c) Gonadotrophs                                                                                                                                                                          |
| Hormone                         | Secrete growth hormone (GH): <ul style="list-style-type: none"> <li>• ↑ secretion → gigantism (before closure of epiphyses) &amp; acromegaly (after closure of epiphyses),</li> <li>• ↓secretion -&gt; dwarfism.</li> </ul> | Secrete prolactin (lactogenic-hormone) → milk secretion. | Thyroid stimulating hormone (TSH) (thyrotropin): Stimulates thyroid gland to secrete thyroid hormones (T3&T4). | 1.Adrenocorticotrophic hormone (ACTH): Stimulates adrenal cortex to secrete cortisol. | <div>FSH secreting cells</div> <div>FSH In females →growth of ovarian follicles.</div> <div>LH secreting Cells</div> <div>LH In females ovulation &amp; formation of corpus luteum.</div> |



| (a) Somatotrophs |                                                                          | (b) Mammotrophs                                                                                                      | (a) Thyrotrophs                                                                        | (b) Corticotrophs                                                                                                                               | FSH secreting cells                 | LH secreting Cells                                                                                                         |
|------------------|--------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
|                  |                                                                          |                                                                                                                      |                                                                                        | <p>2.MSH: stimulates melanocytes of skin to form melanin.</p> <p>3.Endorphin → pain killer.</p> <p>4. Lipotropic factor → lipid metabolism.</p> | In males stimulates spermatogenesis | In males: it is called ICSH (interstitial cell stimulating hormone → stimulate interstitial cell of testis → testosterone. |
| Shape            | Spherical cells with central rounded nuclei and acidophilic granules.    | Oval cells with oval nuclei acidophilic granules.                                                                    | Rounded cells with central rounded nucleus.                                            | Oval cells with eccentric nucleus.                                                                                                              | Rounded cells with rounded nuclei.  |                                                                                                                            |
| Reaction         | Give +ve reaction with orange G, so called orangeophils.                 | Give +ve reaction with carmine & called carminophils.                                                                | -----                                                                                  | -----                                                                                                                                           | -----                               |                                                                                                                            |
| EM               | Cells have well developed Golgi, rER, mitochondria & secretory granules. | Cells have well developed Golgi, rER, mitochondria & secretory-granules, which enlarge during pregnancy & lactation. | All cells have mitochondria, well developed Golgi apparatus, rER & secretory granules. |                                                                                                                                                 |                                     |                                                                                                                            |

### N.B

**\*Pregnancy cells:** During pregnancy and after birth and due to high estrogen level, mammotrophs increase in number and size and secrete prolactin which stimulate development of mammary gland during pregnancy and milk secretion after birth.

**\*Castration cells:** On bilateral removal of the testis, gonadotrophs increase in number & size & accumulate basophilic material pushing the nucleus which becomes flat & peripheral → signet ring appearance.



## II. Pars Tuberalis

- \* Upward extension of pars distalis that surrounds the infundibulum.
- \* **Basophilic cells.**
- \* **Arranged in cords or follicles.**
- \* **Unknown function** but some secrete gonadotrophins (FSH & LH).

## III. Pars Intermedia

- \* **Basophilic cells** with granular cytoplasm,
- \* **Arranged in cords or follicles.**
- \* Rudimentary in man. In some species, e.g. amphibians & reptiles, they secrete melanocyte-stimulating hormone (MSH). (In man, MSH is secreted by corticotrophs in pars distalis).

## Neurohypophysis

### I. Infundibulum

- \* Collection of nerve fibers (axons of neurosecretory cells of hypothalamus).
- \* Connect the hypothalamus with pars nervosa,

### II. Pars Nervosa

- \* **Secrete no hormones.**

#### \* Contains:

#### 1. Pituicytes:

- Branched cells
- They are supporting neuroglial cells.

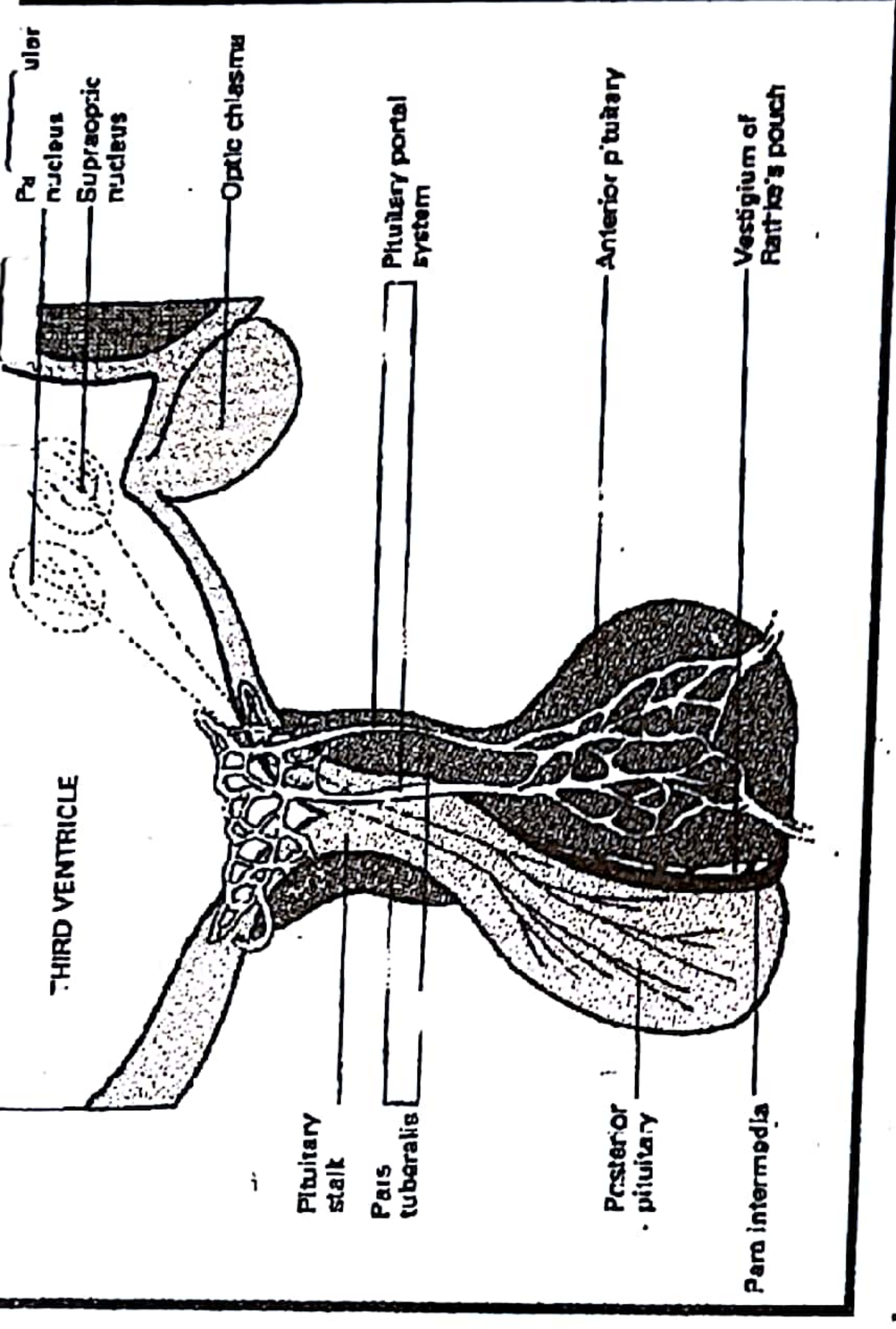
#### 2. Nerve fibers (no nerve cells):

- Axons of secretory cells of hypothalamus.
- They form the **hypothalamo-hypophyseal tract**.
- Carry neurosecretion to blood capillaries.

#### 3. Herring bodies (= acidophilic bodies):

- Accumulated neurosecretion in axon terminals of nerve fibers.
- They contain 2 hormones: oxytocin & vasopressin.

#### 4. Fenestrated blood capillaries: surrounded by Herring bodies.





Function of pars nervosa: Site of storage of  $\rightarrow$  ADH  
 $\rightarrow$  Oxytocin. }

- \*They secreted by supraoptic and paraventricular nuclei of hypothalamus.
- \*They reach pars nervosa via **hypothalamo-hypophyseal tract**.
- \*stored in the axon terminals as **Herring bodies** till needed then released into the capillaries.

**The Neurosecretory Cells of Hypothalamus:**

- \*Neurons present in the paraventricular & supraoptic nuclei of hypothalamus.
- \*secrete the following hormones:

|                                                             |                                                                                                                                                                                                                                  |
|-------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>1. Oxytocin:</b>                                         | <ul style="list-style-type: none"> <li>- Stimulate uterine contractions (in labor).</li> <li>- Stimulate contraction of myoepithelial cells of mammary gland <math>\rightarrow</math> milk ejection during lactation.</li> </ul> |
| <b>2. Vasopressin (ADH):</b>                                | <ul style="list-style-type: none"> <li>-H<sub>2</sub>O absorption in DCT &amp; collecting tubules of kidney.</li> <li>- Vasoconstriction.</li> </ul>                                                                             |
| <b>3. other nuclei release some other hormones such as:</b> |                                                                                                                                                                                                                                  |
| <b>a. Somatotrophin releasina hormone:</b>                  | - stimulates secretion of GH.                                                                                                                                                                                                    |
| <b>b. Somatotrophin inhibiting hormone:</b>                 | - inhibits secretion of GH (somatostatin).                                                                                                                                                                                       |
| <b>c. Thyrotrophin releasing hormone:</b>                   | - stimulates secretion of TSH.                                                                                                                                                                                                   |
| <b>d. Corticotrophin releasing hormone:</b>                 | - stimulates secretion of ACTH.                                                                                                                                                                                                  |
| <b>e. Gonadotrophin releasing hormone:</b>                  | - stimulates secretion of gonadotropins: (FSH&LH).                                                                                                                                                                               |
| <b>f. Prolactin inhibiting hormone:</b>                     | - inhibits secretion of prolactin (dopamine).                                                                                                                                                                                    |

**Blood Supply of Pituitary:**

- Superior hypophyseal arteries supply hypothalamus, stalk & pars intermedia  $\rightarrow$  Iry capillary plexus in infundibulum, join $\rightarrow$  veins in pars tuberalis  $\rightarrow$  rebranch  $\rightarrow$  2ry capillary plexus to supply pars distalis (**hypophyseal portal circulation**).
- Inferior hypophyseal arteries supply pars distalis & pars nervosa.

\*The releasing & inhibiting hormones of the hypothalamus are transmitted from axon terminals to Iry capillary plexus & along the portal circulation to 2ry plexus then to cells of pars distalis to regulate their secretory activity.



# Suprarenal Glands

- Two endocrine glands in contact with upper border of both kidneys.
- Formed of:

(Derived of 2 embryonic sources)  
 1) Mesoderm → Adrenal cortex  
 2) Aneuroectoderm → Adrenal medulla

## I. STROMA:

### A. Capsule:

Thick dense fibrous C.T. capsule, covered with adipose C.T.

### B. Trabeculae:

- \* thin, C.T. cells + fibers.
- \* descend from the capsule to divide the cortex into compartments.

### C. Reticular C.T.:

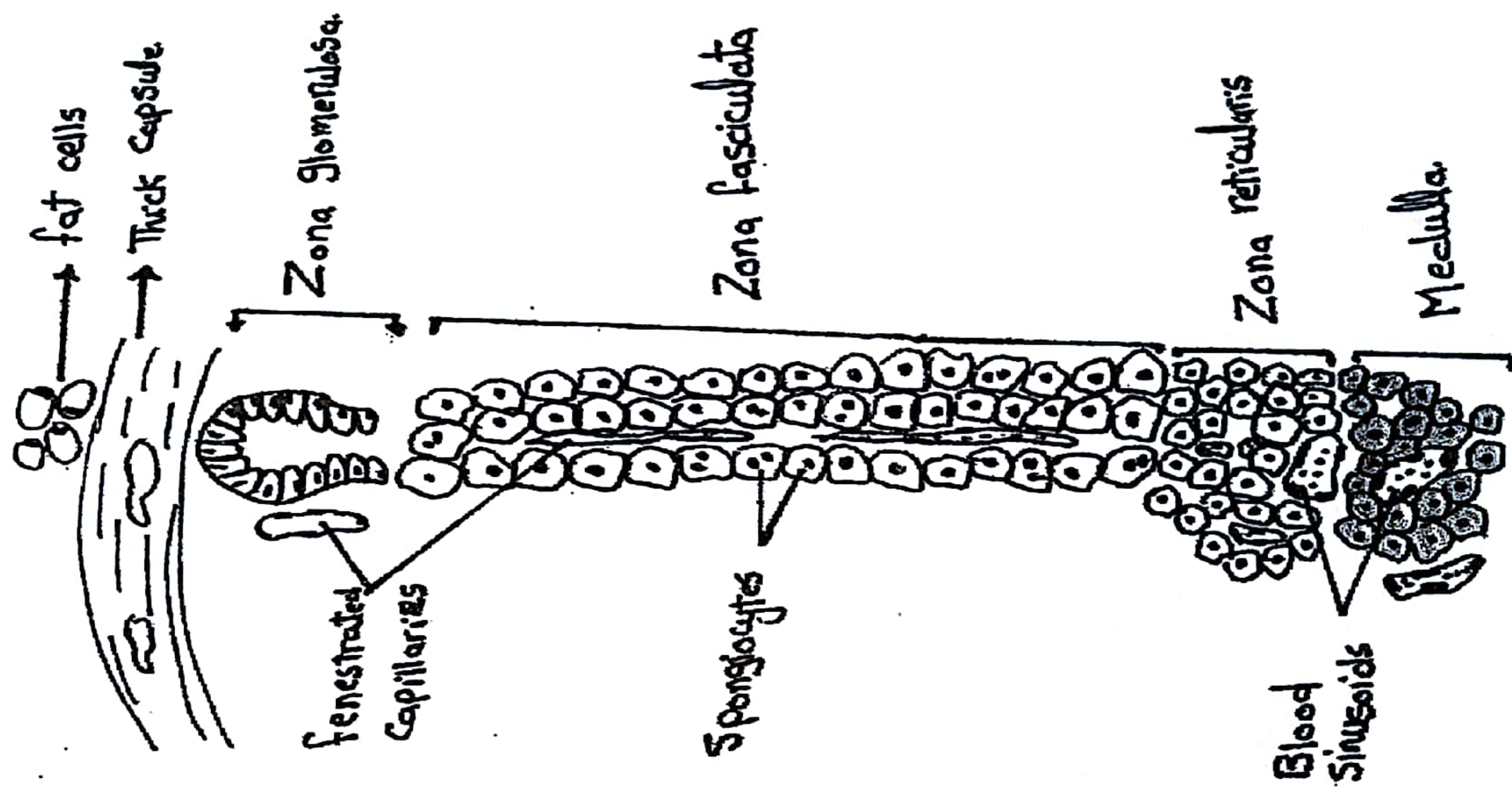
- \* Reticular cells & fibers
- \* present in the background
- \* stained with Ag.

## II. PARENCHYMA:

### A. Cortex:

| 1. Zona Glomerulosa:                                                                                                                                      |  | 2. Zona Fasciculata:                                                                                                                                                        | 3. Zona Reticularis:                                                                                               |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------|--|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| - A narrow zone just under the capsule.                                                                                                                   |  | - The widest zone.                                                                                                                                                          | - The deepest zone.                                                                                                |
| - <u>LM</u> : Formed of columnar cells arranged in arched groups (glomeruli) surrounded by fenestrated capillaries.                                       |  | - Polyhedral cells arranged in straight cords (fascicles), one or two cell-wide, separated by straight fenestrated capillaries.                                             | - Polyhedral cells arranged in branching & anastomosing cords separated by blood sinusoids.                        |
| - Have basal oval (rounded) nucleus.                                                                                                                      |  | - Have central rounded pale vesicular nucleus. Some cells contain 2 nuclei.                                                                                                 | - Have central rounded nucleus.                                                                                    |
| - Pale cytoplasm.                                                                                                                                         |  | - Cytoplasm appears vacuolated, so called spongiocytes.                                                                                                                     | - Cytoplasm is acidophilic.                                                                                        |
| - <u>EM</u> : rich in mitochondria, Golgi apparatus, sER & few fat droplets,                                                                              |  | rich in mitochondria, Golgi apparatus, sER, many fat droplets, cholesterol & vitamin C.                                                                                     | rich in mitochondria, Golgi apparatus, sER & few fat droplets. Lipofuscin pigment is commonly seen in these cells. |
| - <u>Function</u> : secrete mineralocorticoids mainly aldosterone which regulates electrolyte & water balance ( <u>under control of angiotensin II</u> ). |  | Secrete glucocorticoids (cortisol) which regulate lipid, carbohydrate metabolism ( <u>under control of ACTH</u> ). They also anti-inflammatory & immunosuppressive effects. | Secrete androgens & small amount of glucocorticoids ( <u>under control of ACTH</u> ).                              |





## **B. Medulla:**

### **1. Chromaffin cells:**

- Modified sympathetic neurons → lost their processes and became secretory cells.
- Polyhedral cells with central rounded pale nuclei.
- Have basophilic cytoplasm rich in fine granules that stain brown with chromium salts.
- Arranged in branching cords separated by blood sinusoids.
- **E/M:**
  - Cytoplasm shows
    - Mitochondria, rER.
    - Well developed Golgi apparatus
    - & membrane-bound secretory granules.

### **• There are 2 types of cells at ultrastructural (EM) level:**

- a) Adrenalin secreting cells: with less dense & homogeneous granules, i.e. the contents fill the granules.
- b) Noradrenalin secreting cells: with more dense granules & peripheral clear halo beneath the membrane.

The secretory granules also contain opiate-like peptides = enkephalins.

### **2. Sympathetic nerve cells:**

- Stellate nerve cells.
- Innervated by preganglionic sympathetic nerve fibers.
- Scattered between chromaffin cells to stimulate their secretory activity.



### Functions of medulla:

- Secrete adrenalin & noradrenalin in response to stress (fight, flight & fright).
- During normal activity, the medulla continuously secretes small amounts of the 2 hormones.

### N.B. Chromaffin reaction:

- When a fresh section of the suprarenal gland is stained with chromium salts, the medulla stains brown due to presence of adrenalin & noradrenalin.
- Chromaffin reaction is +ve in:
  - Chromaffin cells of suprarenal medulla.
  - Paraganglia.
  - Argentaffin cells of GIT.

### Blood Supply of Suprarenal Gland:

- Three suprarenal arteries (superior, middle & inferior) pierce the capsule -> 3 groups of arterioles (capsular, cortical & medullary)
- The cortical capillaries drain into veins of medulla which join to form suprarenal vein which leaves the gland.

| Differences between suprarenal cortex & medulla.             |        |                                                 |
|--------------------------------------------------------------|--------|-------------------------------------------------|
|                                                              | Cortex | Medulla                                         |
| Mesodermal in origin                                         |        | Ectodermal                                      |
| Formed of 3 zones (glomerulosa, fasciculata & reticularis)   |        | Two types of cells (chromaffin & nerve cells)   |
| Essential to life (corticosteroids).                         |        | Less essential.                                 |
| Secretes mineralocorticoids, glucocorticoids & sex hormones. |        | Secretes adrenalin, noradrenalin & enkephalins. |
| Give -ve chromaffin reaction.                                |        | +ve reaction.                                   |
| Supplied with arterial blood                                 |        | Supplied with arterial & venous blood           |

### Paraganglia:

- Masses of chromaffin cells scattered in close association with the sympathetic ganglia.
- They develop from neuroectoderm (like sympathetic ganglia).
- Give +ve chromaffin reaction.
- Function: secrete adrenalin & noradrenalin.



\*Large endocrine gland

# Thyroid Gland

In the front of the neck.  
Formed of 2 lobes conned by isthmus.

## A. Capsule:

2 capsules:

- Outer false capsule of pretracheal fascia.
- Inner true capsule C.T cells + fibers, firmly adherent to the gland.

## B. Trabeculae:

- Thin, divide the gland into lobes & lobules.
- C.T. cell + fibers.
- Carry blood vessels.

## C. Reticular C.T.:

- Reticular cells + fibers
- In the background, stained with silver (Ag)

## II. PARENCHYMA:

### A. Thyroid Follicles:

- The structural & functional units of the gland.
- Rounded or oval in shape, surrounded by fenestrated blood capillaries.
- Lumen of the follicle filled with acidophilic colloid material (iodinated glycoprotein).
- Lined with cubical epithelium, resting on thin basement membrane. There are 2 types of cells:

| The cell  | 1. Follicular cells (98%) (endodermal):                                                                                                                                                                                                                         | 2. Parafollicular (C-cells) (2%)                                                                                                                                                                                                                      |
|-----------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| LM:       | <ul style="list-style-type: none"><li>- cuboidal cells with basophilic cytoplasm &amp; central rounded nuclei.</li><li>- in hyperthyroidism → cells become columnar.</li><li>- in hypothyroidism → cells become squamous.</li></ul>                             | <ul style="list-style-type: none"><li>- Larger cells with paler cytoplasm, so called clear cells (stained with Ag).</li><li>- Present between the basement membrane and follicular cells.</li><li>- Do not reach the lumen of the follicle.</li></ul> |
| EM:       | <ul style="list-style-type: none"><li>- The apex of cells show short microvilli &amp; adjacent cells joined by tight junctions.</li><li>- Have mitochondria, rER, supranuclear Golgi apparatus, ribosomes, apical secretory vesicles &amp; lysosomes.</li></ul> | <ul style="list-style-type: none"><li>- Have mitochondria, rER, Golgi apparatus &amp; basal secretory granules.</li></ul>                                                                                                                             |
| Function: | Secrete thyroid hormones (T3 & T4) under control of TSH.                                                                                                                                                                                                        | Secrete thyrocalcitonin (belong to APUD cells) → ↓ blood calcium.                                                                                                                                                                                     |



## B. Interfollicular Tissue:

- In-between thyroid follicles,
- Reticular C.T., interfollicular cells (tangentially cut follicles), occasional C-cells & fenestrated blood capillaries.

### Synthesis of Thyroid Hormones:

1. The cell can pick up amino acids & iodide from blood.

\* Synthesis of protein in rER.

\* Addition of carbohydrate in Golgi apparatus → glycoprotein in secretory vesicles (which travel to apex)

\* Exocytosis of glycoprotein in the secretory vesicles into the lumen.

\* Iodide (picked from blood) is oxidized by peroxidase into iodine which is liberated into lumen.  
\* Extracellular iodination of glycoprotein → iodinated thyroglobulin stored as colloid.

\* Pinocytosis of colloid → pinocytic vesicles.

\* Pinocytic vesicles fuse with lysosomes & the hydrolytic enzymes hydrolyze colloid into T3 & T4 which are released into blood.

### Parathyroid Glands

Four small endocrine glands at the back of the thyroid gland.

#### I. STROMA:

A. Capsule:

C.T., cells & fibers, thin.

B. Trabeculae:

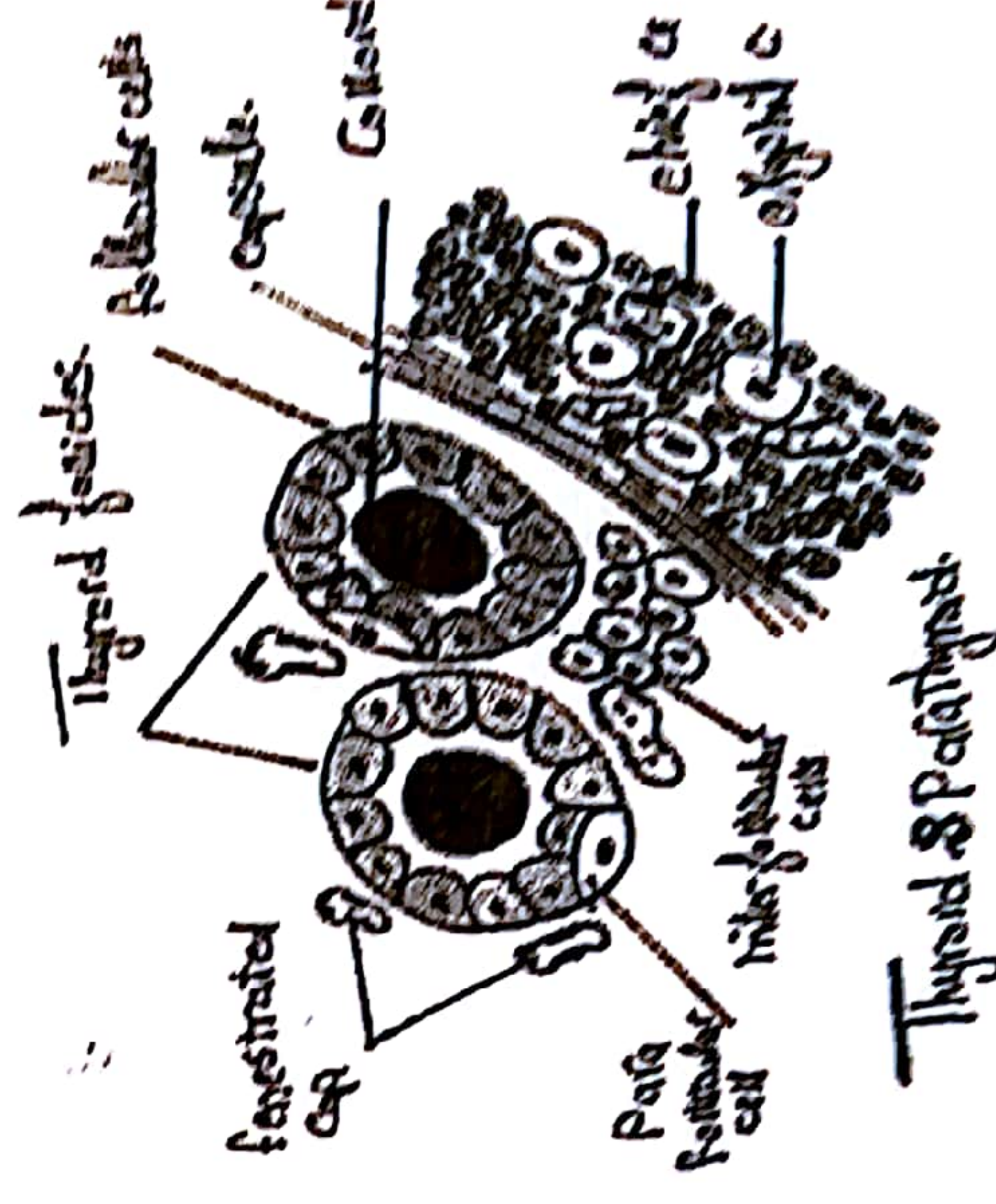
C.T. cells & fibers, thin, divide the gland into incomplete lobules, carry blood vessels.

C. Reticular C.T.

reticular cells & fibers in the background stained with Ag.

#### II. PARENCHYMA:

- Cells arranged in anastomosing cords separated by fenestrated capillaries,
- Two types of cells: (a) chief cells, (b) oxyphil cells,





Chief and oxyphil cells of parathyroid gland.

| (a) Chief cells                                                     |  | (b) Oxyphil cells                                  |
|---------------------------------------------------------------------|--|----------------------------------------------------|
| More numerous & small                                               |  | Less numerous but larger. Number increase with age |
| Polygonal cells with central rounded nuclei                         |  | Oval or rounded cells with eccentric nuclei        |
| Have basophilic cytoplasm & vesicular nucleus                       |  | Deeply acidophilic cytoplasm & dark nucleus        |
| Fine secretory granules                                             |  | Acidophilic granules                               |
| EM: rich in mitochondria, rER, Golgi apparatus & secretory granules |  | EM: mitochondria                                   |
| Function: secrete parathyroid hormone → ↑↑ blood calcium            |  | Function not yet known                             |

**Pineal Body (Epiphysis Cerebri)**

- \*Cone-shaped neuroendocrine gland derived from neuroectoderm.
- \*Attached to third ventricle by pineal stalk.
- \*Covered with pia mater from which septa containing B.V., unmyelinated nerve fibers arise to divide the gland into incomplete lobules. Formed of:

**1. Pinealocytes:**

- Large branched cells with long tortuous processes which end by dilatations on blood capillaries in the vascular septa.
- Have large pale nucleus with clear nucleolus.
- Have basophilic cytoplasm rich in mitochondria, Golgi apparatus, rER, secretory granules.
- Innervated by unmyelinated nerve fibers, some form synapse with pinealocytes. Synaptic vesicles containing noradrenalin are seen in these nerve endings.

- **Function:** secrete:

**1. Serotonin** (at day time).

**2. Melatonin** (at night):

- Regulates gonadal function preventing precocious puberty.
- Regulates sleep rhythm,
- Antioxidant (protection of body cells).

**2. Astrocytes:** neuroglial supporting cells between pinealocytes with darker nuclei & long processes and many intermediate filaments.

**3. Fenestrated blood capillaries.**

**4. Brain sand (psammoma bodies, corpora aranacea):** calcified concretions (calcified secretory products in concentric layers) which ↑ with age (landmark in X-ray to localize any mass in the brain which may displace its position).



## APUD Cells (DNES)

- \*Amine Precursor Uptake & Decarboxylation cells.
- \*Most of them can take up amine precursors & have amino acid decarboxylase activity.
- \*Can be stained with Ag, so called argentaffin cells.
- \*Derived from neuroectoderm, so also called diffuse neuroendocrine system (DNES).
- \*Considered as highly modified neurons. Their secretions act as hormones or neurotransmitters.

EM: They have ribosomes, rER, basal secretory granules or synaptic vesicles.

### Sites:

1. Respiratory tract: between cells of respiratory epithelium & secrete serotonin, calcitonin, catecholamines & enkephalins.
2. GIT: stomach, intestine, pancreatic duct & common bile duct. They are called enteroendocrine cells and include:
  - G-cells → gastrin.
  - K-cells → antigastrin (gastrin-inhibitory peptide, GIP).
  - A-cells → glucagon.
  - D-cells → somatostatin.
  - EC-cells → serotonin.
  - S-cells → secretin.
  - E-cells → endorphin.
  - N-cells → neurotensin.
  - MO cells → motilin.
  - I-cells → cholecystokinin-pancreozymin.

3. Pancreas: islets of Langerhans.
4. Suprarenal medulla: chromaffin cells → catecholamines.
5. Thyroid gland: C-cells → calcitonin.
6. Pituitary gland: corticotrophs → ACTH & MSH.
7. Hypothalamus: neurosecretory cells.
8. Kidney: juxtaglomerular cells → renin.
9. Prostate: PEP cells (prostatic endocrine paracrine cells) → serotonin.
10. Skin: Merkle's cells.



### **Medical applications:**

-Tumors of the adenohypophysis are usually benign. These tumors produce excess amounts of hormones that cause clinical symptoms.

Clinical diagnosis can be confirmed by immunocytochemical methods following surgical removal.

-Because of the negative feedback mechanism controlling the adrenal cortex, patients treated with corticoids for long periods should never stop taking these hormones suddenly as ACTH secretion is inhibited and the cortex is not induced to produce corticoids.

**Pheochromocytoma:** a tumor of cells of the adrenal medulla, characterized by excess production of catecholamines with life threatening hypertension, cardiac arrhythmias and anxiety.

-A diet low in iodine hinders the synthesis of thyroid hormones, causing increased secretion of TSH and compensatory growth of the thyroid gland a condition known as iodine deficiency goiter. Goiters are endemic in some regions of the world where dietary iodide is scarce.

**-Hyperparathyroidism:** blood  $\text{Ca}^{2++}$  increased, bone showed increased osteoclasts and bone cavities. Bones of patients with this disorder are more prone to fractures.

**Hypoparathyroidism:** blood  $\text{Ca}^{2++}$  decreased, bones become denser and more mineralized. This condition causes spastic contraction of skeletal muscles (Tetany).



## Testis

- A compound tubular, mixed gland w develops retroperitoneally then migrate to Scrotum. Scrotum = pouch of skin e' no fat to maintain the testis at  $2-3^{\circ}\text{C}$  below body temp. (essential for spermatogenesis), many eccrine sweat glands & dartos muscle (haphazardly arranged) its contraction leads to wrinkling of scrotal skin

### Stroma:

- \* Capsule: Formed of 3 coats:

#### (1) Tunica Vaginalis:

a peritoneal fold brought down during descent of testis to scrotum Formed of: visceral & parietal layers: lined e' s.sq. mesothelium & contains watery fluid → lubricant to allow free movement of testis.

#### (2) Tunica Albuginea:

A c.t. capsule, thickened posteriorly to form → mediastinum testis.

#### (3) Tunica Vasculosa: vascular c.t. lining t. albuginea & Septa.

### \* Trabeculae:

arise from mediastinum testis to divide the testis → 250 compartment [lobules]

Each lobule contains 1-4 Seminiferous tubule + c.t. rich in bl. vs, ns + l. vs + interstitial cells of Leydig.

### \* Ret.c.t

### Parenchyma:

(a) Exocrine part = Seminiferous tubules → sperms

(b) Endocrine part = Interstitial cells of Leydig → testosterone.

### The Seminiferous Tubules.

- No: 250-1000 convoluted tubules - 30-70 cm long & 200  $\mu\text{m}$  in diameter
- lined e' stratified epith = Spermatogenic epith. formed of 2 types of cells I + II

### I. Sertoli Cells:

- the main cells till puberty but after puberty = only 10% of the cells lining the tubules
- not affected by factors affecting spermatogenic cells.

#### \* L.M.

- tall pyramidal cells w extend from the b.m. to the lumen
- have indistinct cell boundaries
- have pale vesicular oval or triangular nucleus e' clear nucleolus.
- have pale acidophilic cytoplasm.

#### \* E.M.

- numerous mitochondria, well developed G.A, abundant s.ER, few rER, lysosomes & free ribosomes & many lipid droplets - well developed cytoskeleton of microfilaments & microtubules to help upward movement of spermatogenic cells towards the lumen.
- the lateral border contain deep invaginations or pockets in w spermatogenic cells lie.
- At the basal parts cytoplasmic extensions from adjacent cells are joined by tight junction [Occluding J.] to divide the seminiferous tubule into basal compartment & adluminal compartment.
- Each Sertoli cell supports 30-50 spermatogenic cell at diff. stages of development.



## • Functions of Sertoli Cells:

### 1. Supportive & nutritive functions:

- Spermatogenic cells are present inside pockets (invaginations) in their lat. walls.
- Sertoli cells regulate passage of nutrients to spermatogenic cells & transport of waste products to bl. & lymph outside the seminiferous tubules.

### 2. Phagocytic function:

- digest residual bodies resulting from spermiogenesis.
- ↳ degenerating cells w fail to complete spermatogenesis.

### 3. Secretory function:

- In  $\sigma$  Embryo: [about 8<sup>th</sup> or 9<sup>th</sup> week]:  
secrete Müllerian inhibitory substance: inhibits development of Müllerian duct system.
- In prepubertal testis: secrete a substance  $\rightarrow$  give  $\sigma$  embryo  $\rightarrow$  prevent meiosis of spermatogenic cells.
- In postpubertal testis: secrete:
  - testicular fluid: w carry immotile sperms to the genital ducts. (rich in Fructose)
  - A.B.P. [Androgen Binding ptn] (under control of FSH). A.B.P. combines w testosterone & transport & concentrate it to stimulate spermatogenesis in the tubules
  - Inhibin: inhibit synthesis & release of F.S.H. i.e. inhibits spermatogenesis.

### 4. Form Blood Testis barrier:

The barrier w separates tissue fluid outside the seminiferous tubules from spermatogenic cells inside it. Formed by: tight junction bet. cytoplasmic extensions at the basal parts of Sertoli cells dividing the tubules into:

- a. Basal compartment (under the barrier): containing only spermatogonia.
- b. Adluminal " " (above " " ): " " the rest of spermatogenic cells.

So, tissue fluid can penetrate the b. memb. to reach spermatogonia in the basal compartment & cannot reach the rest of the spermatogenic cells in the adluminal " " except through the barrier (Sertoli cells).

The newly formed 1-2  $\mu$  Spermatocytes disrupt the junction forming the barrier to reach the adluminal compartment after a new junction is formed.

### Functions of Blood testis barrier:

1. Selection of nutrients & hormones needed for differentiation of spermatogenic cells.
2. Isolation & protection of spermatogenic cells from any damaging subs in the blood
3. Create special environment in the adluminal compartment rich in  $\text{Na}^+$ ,  $\text{K}^+$  & A.B.P. needed for proper spermatogenesis.
4. Prevent autoimmune reaction: As spermatogenic cells are formed after puberty, so body's immune system consider them as antigen & produce antibodies (antisperm Immunoglobulins). B.l. test. Barrier prevent passage of these Abs. to sperms.



## (1) Spermatogonia: 21. Spermatogenic Cells:

Small cells ( $12\mu\text{m}$ ) rounded cells e' rounded nuclei e' diploid No of chromosomes ( $44+XY$ ). They lie in one or 2 layers on the basement memb. 3 types:

- a. Dark type A: have dark nuclei = Precursor cells: they divide to give 1 additional dark type A (reserve cells) + 1 pale type A = cycling cells.
- b. Pale type A: have pale nuclei = (cycling cells): divide by mitosis to give:
- c. Type B: Similar to pale type A but larger: divide, grow in size & differentiate into:

## (2) 1<sup>st</sup> Spermatocytes:

- The largest cell ( $18\mu\text{m}$ ) arranged in 2 or 3 layers.
- have largest rounded nucleus e' diploid no. of chromosomes = 46. e' prominent coiled chromosomes as they enter the prophase of 1<sup>st</sup> meiotic division w is very long (22 days). By the end of 1<sup>st</sup> meiotic division they give rise to 2<sup>nd</sup> Spermatocytes.

## (3) Secondary Spermatocytes:

- Smaller cells e' smaller nuclei
- have haploid No of chromosomes (23) ( $22+X$  or  $22+Y$ )
- difficult to be seen in section as they are short lived & rapidly enter 2<sup>nd</sup> meiotic division to give spermatids.

## (4) Spermatids:

- Very small cells ( $8\mu\text{m}$ ) e' central dark nuclei near the lumen of the tubules.
- Each spermatid by spermiogenesis → mature sperm.  
e' no further division

## (5) Spermatozoa: ( $60\mu\text{m}$ long) formed of:

Head + tail [neck, middle piece, principal piece & end piece] covered e' cell memb & little cytoplasm.

- Head: ( $5\mu\text{m}$ ) = flat, elongated formed of condensed nucleus. It's ant. 2/3 is covered e' head cap [acrosome] rich in hydrolytic enzs. to facilitate penetration of oocyte.
- Neck: short segment: contain 2 centrioles.
- Middle piece ( $5\mu\text{m}$ ) = flagellar axoneme = 9 peripheral doublet microtubules + 2 central singlets surrounded by supporting fibres then by mitochondrial sheath.
- Principal piece ( $40\mu\text{m}$ ) the flagellar axoneme surrounded by supporting fibres.
- End piece ( $10\mu\text{m}$ ) = axoneme only.

## Spermatogenesis

The process of formation of sperms:

Starts at puberty under control of FSH.

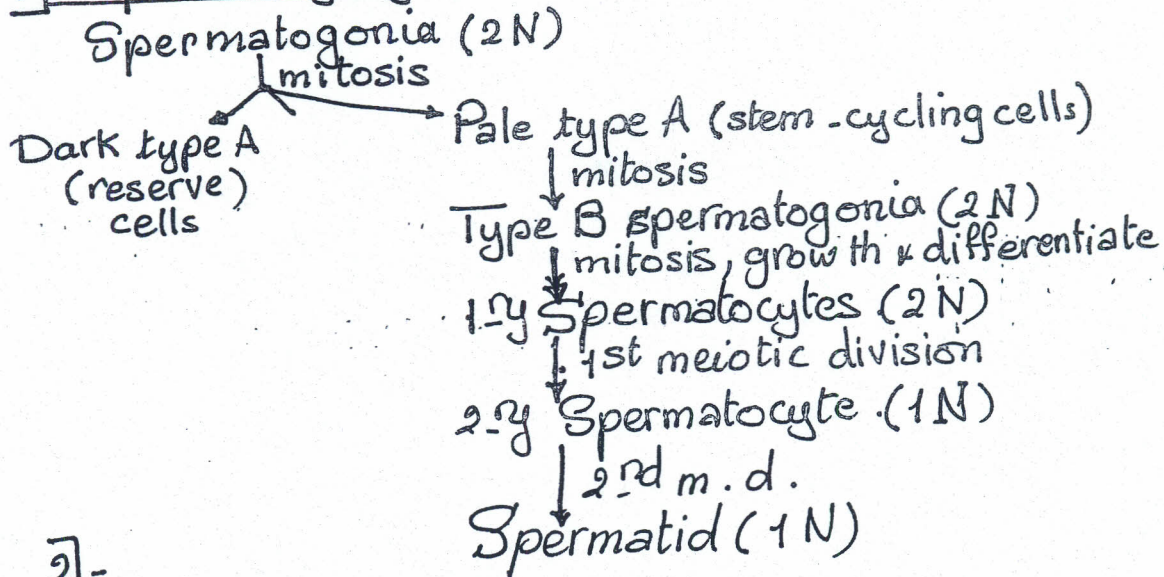
lasts about 64 → 70 days. 2 Stages:

1] Spermatocytogenesis.

2] Spermiogenesis.



## 1] - Spermatocytogenesis:



2]-

## Spermiogenesis:

The transformation of spermatid into sperm by metamorphosis & cell division.

Includes 3 phases:

**A. Golgi phase:** rER forms hydrolytic enzs. w are modified & packed in G.A. From w memb. bound proacrosomal granules fuse to form a single granule bounded by acrosomal vesicle at one pole while the 2 centrioles migrate to the opposite pole.

### B. Acrosomal phase:

- The nucleus elongates, flattens & become condensed.
- the acrosomal vesicle enlarge to cover the ant.  $\frac{1}{2}$  of the nucleus & form acrosomal cap.
- One centriole forms flagellar axoneme w become surrounded by supporting ptn. fibres
- mitochondria aggregate around the 9 fibres forming the middle piece where flagellar movement is generated.

### C. Maturation phase:

- the acrosomal cap enlarge to cover the ant.  $\frac{2}{3}$  of the nucleus  $\Rightarrow$  acrosome. w contains (acrosin) hyaluronidase, acid-phosphatase & proteases. When a sperm contacts an oocyte, these enzs digest Corona radiata then zona pellucida to facilitate fertilization.
- Excess cytoplasm pinch off as residual bodies phagocytosed by Sertoli cells.
- newly formed sperms separate from apices of Sertoli cells & lie free in the lumen. (a process called spermiation).

### • Acrosomal Reaction:

When a sperm encounter an oocyte, the outer membrane of the acrosome fuses w the cell memb. of the sperm at several sites liberating the enzs in the extracellular space [1st step of fertilization]

### • Immotile Cilia Syndrome:

lack of ptns. needed for ciliary & flagellar motility  $\rightarrow$

$\rightarrow$  immotile sperms  $\rightarrow$  infertility of the affected men.

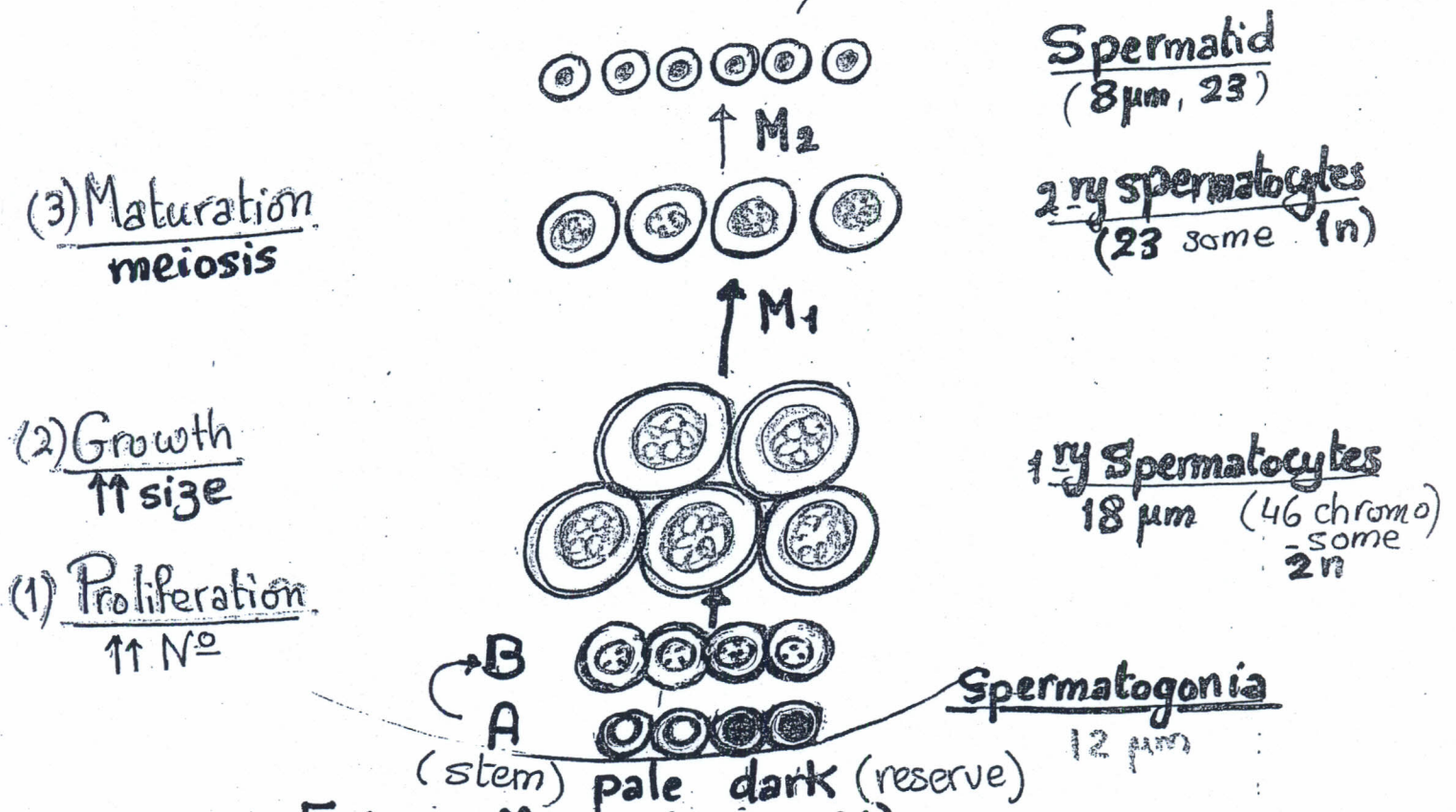
$\rightarrow$  " " cilia of resp. epith  $\rightarrow$  chronic respiratory infections.



# Spermatogenesis

- 5 -

I. Spermatocyto-genesis (1) + (2) + (3) + II. Spermiogenesis   
 metamorphosis & out cell division Sperm



## Factors affecting Spermatogenesis

(5)

1. Temperature: 35°C is the suitable temp. controlled by:

- presence of testis in scrotum
- pampiniform plexus of veins surround the testicular artery → heat exchange system to lower the temp. of arterial bl. supply of the testis.
- evaporation of sweat from scrotum.
- contraction of cremasteric muscle pulls testis towards inguinal canal in cold weather to ↑ temp & vice versa in hot weather.
- contraction of Dartos ms → wrinkling of scrotal skin ↓ sweat evaporation
- In hot weather it relaxes → stretching " " " ↑ sweat evaporation

## 2. Hormones:

- L.H. (ICSH) stimulate leydig cells to secrete testosterone.
- Testosterone: stimulate spermatogenesis.
- F.S.H.: stimulate Sertoli cells to produce ABP w accumulate testosterone in the Seminiferous tubules.
- Inhibin: inhibit F.S.H. secretion, so inhibits spermatogenesis.

3. Vitamins: vit. A & E are needed for spermatogenesis.

## 4. Other inhibiting Factors:

Toxins alcoholism, irradiation, drugs, malnutrition suppress Spermatogenesis



(N.B) Cryptorchidism = failure of descent of testis to scrotum → testicular temp is  $37^{\circ}\text{C}$  this inhibits spermatogenesis & might lead to sterility. So newborns must be checked for descent of testis in scrotum for rapid treatment.

Varicocele = abn. dilatation of pampiniform plexus of veins → fail to  $\downarrow$  testicular temp. affecting quantity & quality of sperms.

### Interstitial tissue

The spaces bet. seminiferous tubules: contain loose c.t. rich in fibroblasts, macrophages, mast cells + fenestrated capillaries + nerves + lymph vessels + myoid cells + Leydig cells

Myoid cells = flattened contractile cells that surround the tubules. Their contractions propel the non-motile sperms towards rete testis

### Interstitial Cells of Leydig:

- endocrine cells separated by fenestrated caps. present in bet. seminiferous tubules
- \* • L.M. 14–21  $\mu\text{m}$   
rounded cells w/ central rounded pale vesicular nucleus & clear 1–2 nucleoli  
cytoplasm acidophilic & many fat droplets.
- E.M. characters of steroid secreting cells: extensive SER, mit. G.A + many fat droplets
  - ↳ Reinke's crystalloid inclusions of unknown nature seen after puberty & 1st age
  - ↳ lipofuscin granules (esp in old men)
- \* • Function: secrete testosterone under control of L.H.
  - testosterone → stimulates spermatogenesis.
  - appearance of 2<sup>nd</sup> sex characters.
- Leydig cells resist injurious factors e.g. high temp., X-ray .... etc.



## Genital Ducts

### I. Intratesticular ducts:

- ① Tubuli recti: straight tubules at the end of the seminiferous tubules, lose spermatogenic cells & lined only by **Sertoli cells** w/ abruptly → **cuboidal cells**.
- ② Rete testis: network of tubules in mediastinum testis lined by **cuboidal cells** then **cylindrical cells**.

(N.B) the beginning of vasa efferentia is intratesticular but its main part is extratesticular.

### II. Extra testicular ducts:

1. Vasa Efferentia: 10-20 tubules that enter the head of epididymis lined by **testis-tubed Epith.** = tall col. cil. cells alternating w/ low col. non-ciliated cells. rests on a clear b.m. surrounded by c.t. & smooth ms. fs.

Functions: ① their cilia propel sperms towards epididymis helped by peristaltic contract of their ms. ② Non-ciliated cells absorb some testicular fluid.

### 2. Epididymis:

- 4-6 meters long, 400  $\mu$ m in diameter, highly convoluted → compact organ 7.5 cm long
- Formed of: Head, body & tail. Vasa efferentia enter the head while the tail ends in vas deferens.
- lined by: **pseudo stratified col. cil & non-motile (stereocilia)** = long microvilli resting on clear basement membrane surrounded by c.t. & smooth ms.
- E.M.: cells are rich in rER, well developed G.A, lysosomes + coated vesicles.
- Functions:
  1. Absorption of Testicular Fluid.
  2. phagocytose & digest residual bodies of spermiogenesis & degenerated sperms.
  3. Secrete glycoproteins w/ help maturation of sperms.
  4. the peristaltic contraction of their muscles propel sperms to the vas.
  5. Storage & maturation of sperms.

### (N.B) Capacitation:

It is the ability of sperms to reach full maturity, motility & power of fertilization through a series of biochemical reactions. Starts in epididymis, reach its peak in Fallopian tube near the Oocyte.

### 3. Vas deferens:

Muscular tube 45 cm long, 3 mm in diameter, starts at tail of epididymis & become dilated near its end → ampulla of vas. Formed of:

1. Mucosa: a. pseudo stratified col. cil & stereocilia w/ disappears upwards.  
b. c.t. corium rich in elastic fibres.

2. Musculosa: 3 layers: inner & outer long & thick middle circ. l.

3. Adventitia: loose c.t. rich in elastic fs.

Functions: contraction of the thick musculosa → propel sperms to urethra during <sup>ejaculation</sup>

### 4. Ejaculatory duct:

1 cm Formed by union of the ampulla of vas & duct of the seminal vesicle. Opens into the prostatic urethra. lined by ps. st. col. (non-cil) & no muscles in its wall.

### 5. Urethra.



## Spermatic Cord

(7)

Contains: 1. Vas deferens. 2. Testicular artery 3. lymph vs. 4. nerves  
5. pampiniform plexus of veins. 6. Cremasteric ms.: long. involuntary skeletal ms.

## ♂ Accessory Genital Glands

### (1) Seminal Vesicle

2 tubes (15 cm long) coiled on itself → 5-6 cm long body = 3 layers:

**A. Mucosa**: highly folded =

a. ps. st. col.: by E.M. = ptn. secreting cells <sup>mit, rER</sup> GA, secretory vesicles. The height & degree of activity depends on testosterone.

b. lamina propria = c.t. rich in elastic fibres.

**B. Musculosa**: inner circular & out. long.

**C. Adventitia**: loose c.t. rich in elastic fibres.

**Functions**: 1. Form 80% of the seminal fluid w̄ is viscid & yellow (lipochroma pig.).  
2. their secretion is rich in spermatozoa-activating substances e.g. fructose, d.as. ptns., citric A, ascorbic A + prostaglandins & fibrinogen (coagulates semen after ejac.).  
3. Fructose is the main nutrient for sperms & give energy for their motility.  
4. Contraction of their muscles propel the secretion into the ejaculatory duct.

### (2) Bulbo-urethral [Cowper's] glands

2 Compound tubuloalveolar glands (each 3-5 mm in diameter). Present behind the membranous urethra where their ducts open. The acini are lined e' s. cuboidal or s. col. epith w̄ secrete mucous.

The c.t. septa dividing the gl. into lobes & lobules contain **skeletal & sm.ms**

**Function**: secrete clear mucous (rich in sugars) w̄ precedes the semen.

It has a lubricating function.

## Prostate

**def.** Exocrine, comp. tubulo-alveolar gl. around the neck of Ur. bladder

### Stroma:

1. **Capsule**: thick & fibromuscular (rich in sm.ms. & fs).

2. **Trabeculae**: thick, fibromuscular. descend from the capsule to divide the gl. into lobes & lobules.

3. **Ret. c.t.**: ret. cells & fibres in the background. stained e' Ag.

**Parenchyma**: acini + ducts.

1. **Prostatic acini**: 30-50 arranged in 3 concentric groups around the urethra:

a. **Mucosal Group** (central zone):

Small acini around the urethra where they open directly or by short ducts

b. **Submucosal group** (transition zone):

Medium sized w̄ open by short ducts in the postero-lat. aspect of the urethra

c. **Main group**: (peripheral zone):

Large-sized acini (= 70% of the gl.) w̄ open by long ducts in the post. aspect of urethra



\* The acini are lined e' s.col. or ps.st.col. epith e' unclear b.m. & c.t. lamina propria  
 N.B. the height of epith. is controlled by the level of testosterone. inadequate level → cuboidal epith (usually in old age).

by E.M: cells show picture of ptn-secreting cells: many mit, well developed G.A. r.ER + secretory granules.

\* the lumen of the acini frequently show small mass of glycoproteins (usually calcified) = Corpora amylacea or prostatic concretions Me' age. (unknown significance)

2. Prostatic ducts: lined e' s. cuboidal or s.col. epith.

### Functions:

1. produce thin milky prostatic fluid w give the semen its characteristic Odour
2. the secretion is rich in acid phosphatase, amylase + fibrinolysin w liquify the coagulated semen after its deposition in the vagina to allow free movement of the sperms.

### N.B.

\* the mucosal & submucosal groups are the site of benign hyperplasia in old age e' enlarged acini w compress the urethra → difficult micturation & urine retention.

\* the main group: is a major site for cancer prostate w is discovered when advanced being far from the urethra.

\* Prostatic surface antigen (PSA) is a product of the prostate secreted into bl. It's serum level rises in cancer prostate. So it is useful for diagnosis & follow up of the patients

Semen = the thick white fluid released during ejaculation. -

= Sperms + seminal fluid (♂ accessory gls).

Semen analysis: test to measure vol., viscosity, liquification time  
 N° & motility of sperms.

Normal values: vol. = 1.5 - 5 ml N° 20 - 150 million/ml. ≥ 60% normal shape & forward motility.



## The Penis

-9-

Copulatory Organ covered e' skin (has hairs only at its root) e' no subcutaneous fat: to allow free movement of skin during intercourse. Glands of Littre are present along its whole length (secrete mucous) & open in the urethra.

• Formed of 3 Corpora := erectile tissue =

2 Corpora cavernosa & 1 Corpus spongiosum (through w the penile urethra runs). Corpora cavernosa are covered by thick dense c.t. = Tunica albuginea. While corpus spongiosum is covered e' thin T. albuginea.

The Tunica albuginea is surrounded by fascia penis (under the skin)

• At its end the corpus spongiosum expands → **glans penis**.

The erectile tissue =

Connected vascular spaces (lined e' endothelial cells) These spaces are empty in flaccid penis & filled e' blood in erected penis. They are separated by smooth muscles, collagen & elastic fs. Corpus spongiosum is surrounded by more elastic fibres than corpora cavernosa.

Blood Supply of penis:

Dorsal & deep arteries. The deep artery gives 2 branches:

- ↳ nutritive → supply O<sub>2</sub> & nutrition.
- ↳ helicine a. → empty in the cavernous bl. spaces.

- Helicine arteries are spiral in flaccid penis & straight in erected penis.

- Arteriovenous shunts: connect the Helicine arteries e' the deep dorsal veins. They are the normal route of blood flow in the flaccid penis.

Mechanism of erection

\* the parasympathetic causes:

- ① Closure of A-V shunts, so bl. in helicine as is diverted to the bl. spaces
- ② Relaxation of the sm.ms in:
  - (a) dorsal, deep & helicine as → ↑↑ bl. flow to the penis.
  - (b) trabeculae bet. the cavernous spaces → their distension.
- ③ The filled cavernous spaces compress the veins against the dense tunica albuginea blocking outflow of bl., so it is trapped in the spaces → rigid & erected penis.

Mechanism of ejaculation

\* the sympathetic causes:

- ① Opening of the A-V shunts so bl. passes directly to the deep vs.



2

## ② Contraction of the sm.ms in:

- a) dorsal, deep & helicine as  $\rightarrow \downarrow \downarrow$  bl. flow to the penis.
  - b) trabeculae  $\rightarrow$  preventing distension of the cavernous spaces.
- This lowers the press. on the veins  $\rightarrow$  draining the bl. from the penis  $\bar{w}$  returns to the flaccid state.

(N.B) Corpus spongiosum does not become as rigid as corp. cavernosa during erection as tunica albuginea is thin & e' more elastic fs to avoid compression of the penile urethra during ejaculation

(V.B) Glans penis is covered e' a fold of skin prepuce rich in elastic fs. to retract during intercourse. The operation by  $\bar{w}$  prepuce is removed = circumcision.

**Impotence** = inability to achieve erection. Causes:

- a) - temporary: psychological or drugs e.g. alcohol. or
- b) - permanent: lesion in sp. cord or brain, diabetes mellitus & Parkinson's disease.



# ♀ Genital System

-1-

## The Ovary

Formed of:

### [1] Germinal Epith:-

Simple cubical w gradually e'  $\uparrow$  age change into s. sq.

The name is wrong as it does not give ova.

[2] Tunica Albuginea = dense fibrous c.t. under the germinal epith.

[3] - Outer cortex = Stroma + Ovarian follicles.

[4] - Inner Medulla = highly vascular loose c.t.

Bl. vs. ns. & lymph vs. enter & leave at the ovarian hilum.

### Cortical Stroma:

Spindle shaped fibroblast like cells on a background of collagen & reticul. fs.

Collagen fibres  $\uparrow$  e' age (maximum at menopause). Stromal cellularity is hormone dependant.

Functions of stromal cells  $\left\{ \begin{array}{l} \text{support developing ova.} \\ \text{give theca folliculi cells.} \\ \text{secrete } \text{♀} \text{ hrs. (estrogen \& androgen)} \end{array} \right.$

### Ovarian Follicles

present in the cortex. 5 types:

#### [1] Primordial Follicles:

- Just under tunica albuginea. Formed bet. 6<sup>th</sup> & 9<sup>th</sup> month of fetal life.

- formed of 1- $\gamma$  Oocyte (25  $\mu$ m) surrounded by 1 layer of Flat [follicular] cells

1- $\gamma$  Oocyte: have large vesicular nucleus e' clear nucleolus, diploid N<sup>o</sup> of chromosomes. Cytoplasm (Ooplasm) contains: mit., G.A., ER. & lysosomes.

#### [2] Primary Follicles:

At puberty, primordial follicles  $\xrightarrow{\text{FSH}}$  1- $\gamma$  follicles. 2 types:

##### (a) Unilaminar 1- $\gamma$ Follicles:

- 1- $\gamma$  Oocyte  $\uparrow$  in size (40  $\mu$ m) in arrested prophase of 1<sup>st</sup> meiotic division
- Follicular cells become cuboidal.

##### (b) Multilaminar (preantral) 1- $\gamma$ Follicle:

- 1- $\gamma$  Oocyte reaches 50  $\mu$ m. ( $\uparrow$  N<sup>o</sup> of organelles)
- Follicular cells proliferate  $\rightarrow$  many layers of polyhedral cells = granulosa cells
- a thick glycopn. memb. = Zona pellucida (rich in GAGs) forms bet. 1- $\gamma$  Oocyte & granulosa cells (both share in its formation)
- stromal cells around the follicle form concentric layers  $\rightarrow$  capsule [Theca folliculi]
- \* follicles move deep in the cortex.



### 3] 2<sup>nd</sup> [Antral] Follicle :

- 2 -

- liquor folliculi, secreted by granulosa cells accumulate bet. them. It contains GAGs + steroid binding ptns. The spaces containing liquor folliculi unite → 1 large cavity = **Antrum**.
- 1<sup>st</sup> Oocyte enlarge (120  $\mu$ m) & is pushed to one side.
- Theca folliculi differentiates into 

theca externa.  
" interna

### 4] 3<sup>rd</sup> Mature Graafian Follicle :

- Large 2 — 2.5 cm, occupies the whole thickness of cortex & bulges on the surface
- Formed of :
  - a) 1<sup>st</sup> Oocyte: 150  $\mu$ m & just before ovulation changes into 2<sup>nd</sup> Oocyte (1n) = haploid no.
  - b) **Zona pellucida**: thick glycoprotein memb. surrounding the oocyte.
  - c) **Corona radiata**: granulosa cells around the oocyte (become columnar). Have cytoplasmic processes w/ penetrate Z. pellucida & contact microvilli projecting from the oocyte by gap junctions.
  - d) **Cumulus Oophorus**: granulosa cells around the Corona radiata & separating the oocyte from follicular fluid.
  - e) **Granulosa Cells**: 3 — 4 layers of polyhedral cells lining the follicular cavity & secrete follicular fluid & aromatase enz. that converts androgen coming from theca interna → Estrogen
  - f) **Basement memb.** separating granulosa cells from Theca folliculi.
  - g) **Theca Interna**: polyhedral cells enclosing fenestrated capillaries. They either directly secrete **estrogen** or secrete **androgen** by aromatase of granulosa cells → estrogen. By E/M. have features of steroid secreting cells [SER, many mit, fat droplets].
  - h) **Theca Externa**: Compact layer of stromal (fibroblast-like) cells & no secretory function. No clear boundary bet. Th. externa & interna or surrounding stroma.

### 5] Atretic Follicles :

- In each menstrual cycle, about 20 1<sup>st</sup> follicles are activated but only one reaches maturity liberating the Oocyte. the other follicles undergo atresia.
- Atresia occurs at any stage of the developing follicles [primordial, 1<sup>st</sup>, 2<sup>nd</sup> or 3<sup>rd</sup> follicles].
- The Oocyte dies & the surrounding cells degenerate.
- Macrophages phagocytose debris.



- Degenerating primordial or 1ry follicles completely resorb & leaves no scar, but 2ry & 3ry follicles leave a scar of collagen (stays for a long time)

### Fate of M.G.F. [Ovulation]

- High estrogen level  $\rightarrow$  surge of L.H. [at mid cycle = day 14]  $\xrightarrow{\text{stim.}}$  Ovulation
- $\uparrow\uparrow$  pressure of follicular fluid  $\rightarrow$  loosening of granulosa cells  $\rightarrow$  rupture of MGF
- $\rightarrow$  liberation of oocyte into the peritoneal cavity. The oocyte is surrounded by Zona pellucida, corona radiata & cumulus Oophorus & picked up by F. tube. It remains viable for 24 hrs then undergo autolysis.
- Follicular fluid & some blood (from theca interna) are expelled into the peritoneal cavity (pain sensitive)  $\rightarrow$  mid cycle pain.
  - the antrum contains bl. clot.
  - Granulosa cells & theca interna cells  $\rightarrow$  Corpus luteum.

### Corpus luteum

Temporary endocrine gland in the ovarian cortex. Results from ovulation & under effect of L.H. It produces high level of progesterone & moderate estrogen.

#### Formation & structure:

- Release of the follicular fluid  $\rightarrow$  collapse of the follicle & the wall of the corpus luteum is folded. Blood in the cavity  $\rightarrow$  bl. clot w is gradually removed. In animals, the central bl. clot is present  $\rightarrow$  Corpus Hemorrhagicum.
- Granulosa cells:  $\uparrow\uparrow$  in size, become rich in sER, mit., fat droplets & lipochrome pigment  $\rightarrow$  Yellow color in fresh section & called. Granulosa lutein cells  $\rightarrow$  progesterone.
- Theca Interna cells: show EM features of steroid secreting cells [but smaller than granulosa lutein cells, & fewer fat droplets] & called Theca lutein cells  $\rightarrow$  estrogen.

### Fate of Corpus luteum:

- If no pregnancy occurs, L.H  $\downarrow$  & the corpus luteum [C.L. of Menstruation] degenerates within 10-12 days, degenerated cells are phagocytosed by macrophages. Fibroblasts invade it  $\rightarrow$  dense fibrous c.t.  $\rightarrow$  Corpus Albicans
- If pregnancy Occurs: trophoblast of the embryo secrete HCG [similar to LH] w stimulate growth of CL  $\rightarrow$  [C.L. of Pregnancy] w secrete progesterone & estrogen until the placenta is formed. (4-5 months) then degenerates & replaced by Corpus albicans.

#### $\therefore$ Types of Corpora

1. Corpus luteum of menstruation.
2. " " " pregnancy.
3. Corpus haemorrhagicum
4. Corpus albicans.



## Ovogenesis

def.: The process of formation of ♀ gametes. Primordial germ cells [Oogonia] migrate from the endoderm to the ovary of the embryo.

**Proliferation:** [during 1<sup>st</sup> trimester of pregnancy]. Oogonia undergo repeated mitosis → large N° of oogonia (about 7 millions in both ovaries)

**Growth:** [during 2<sup>nd</sup> trimester of pregnancy]

Oogonia ↑↑ in size → 1<sup>ry</sup> Oocytes w enter arrested prophase of 1<sup>st</sup> meiotic division. By 7<sup>th</sup> month of pregnancy, many oocytes undergo atresia such that at puberty both ovaries have 300,000 1<sup>ry</sup> Oocyte

**Maturation:** At puberty, each month, one 1<sup>ry</sup> oocyte (2n) complete 1<sup>st</sup> meiotic division just before ovulation & give 2<sup>ry</sup> Oocyte (1n) & 1<sup>st</sup> polar body. After ovulation, 2<sup>ry</sup> Oocyte enter 2<sup>nd</sup> meiotic division (completed only after fertilization) → mature ovum & 2<sup>nd</sup> polar body.

During the fertile period of ♀ (30-40 years), only 450 Ova are produced & Other oocytes undergo atresia.

- **Anti-Müllerian hr. [AMH]:** Formed by small ovarian follicles to regulate their Growth. It's bl. level is an indicator of remaining follicles (ovarian reserve).
- **Polycystic Ovary Syndrome:** most common disorder 5-10% of ♀s. Cause is uncertain (mostly genetic dis.). ♀ shows multiple ovarian cysts. The cysts are 2<sup>ry</sup> follicles (arrested at early antral stage) & fail to reach mature Oocyte & imbalance in the ♀ sex hrs. leads to irregular menstrual cycle & trouble to get pregnant.



## Fallopian Tube [Oviduct]

10-12cm long. Carry the ovum to the uterus. & site of fertilization.

Anatomically, formed of 4 segments:

Intramural segment: pass through the wall of the uterus.

Isthmus: narrow & thick walled.

Ampulla: thin walled & site of fertilization.

Infundibulum: Have fimbria & open into the peritoneal cavity.

Histologically: wall is formed of 3 layers:

1. Mucosa: folded. Formed of:

(a) S. col. partially ciliated epith.: contain:

- Ciliated cells: → push the ovum.  
→ at ovulation become taller & more ciliated.
- Secretory cells → watery fluid → nutritive to ova.  
→ capacitation of sperms.

(b) Lamina propria of c.t.

2. Musculosa:

Inner circular & out. long. sm. ms. Their peristalsis push the ovum or zygote towards the uterus. [more helpful than cilia].

3. Serosa: = loose c.t covered e' s. sq. mesothelium.

## Modifications in the diff. parts of F. tube:

- mucosal folds are most numerous in the ampulla
- Ciliated cells " " " " " infundibulum.
- Secretory " " " " " intramural part.
- Musculosa is thickest in the isthmus & " " " .

## Tubal Ectopic pregnancy:

The fertilized ovum occasionally implants in the thin walled Fallopian tube (unsuitable for fertilization). It is perforated as the embryo ↑ in size → bleeding in the peritoneum & severe abdominal pain even shock (in cases & severe bleeding).



# Uterus

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Pear shaped organ formed of 3 parts: Fundus, body & cervix. Histologically, fundus & body have the same structure while cervix is different.

## I- Fundus & body of Uterus

Formed of 3 layers:

### 1. Endometrium:

- a. simple col. partially ciliated & partially secretory.
- b. c.t. lamina propria that contains simple tubular gls = endometrial glands lined e' s.col. secretory e' very few ciliated cells.

Functionally, endometrium is divided into:

| a-Functional Zone                                                                                                                                                                                                                                                                                                                | b-Basal Zone                                                                                                                                                                                                                    |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>- the superficial part.</li> <li>- Contains: - Surface epith.</li> <li>+ superficial part of lamina propria.</li> <li>+ " " " endometrial gls.</li> <li>- Supplied by spiral arteries.</li> <li>- marked changes during the menstrual cycle.</li> <li>- the regenerative part.</li> </ul> | <ul style="list-style-type: none"> <li>- the deep part.</li> <li>- the deep part of lamina propria.</li> <li>• " " " " endom. gls.</li> <li>- Straight arteries.</li> <li>- No changes.</li> <li>- the reserve part.</li> </ul> |

### 2. Myometrium:

Very thick, formed of 3 layers: [poorly defined]

- a) Submucosal L. [Stratum Submucosum] = longitudinal sm.ms.
- b) Vascular L. [St. Vasculare] = Circ. & oblique ms → 8-shaped figures around bl.us.
- c) Supravascular L. [St. Supravasculare] = long. sm.ms.

Myometrium is hormone sensitive. During pregnancy it undergoes:

- [hyperplasia (↑↑ N°) & returns to normal (involute) after delivery, in few ws
- [hypertrophy (↑↑ size) After menopause, m.ps atrophy e' ↑↑ fibrous c.t. bet them.

### 3. Perimetrium: loose c.t. covered e' s.sq. mesothelium.

V.B) The spiral & straight as. arise from the arcuate art. in the myometrium

Fibroids Liomyoma = the most common benign tumor in ♀ = tumor of sm.ms of the myometrium.



## II-Cervix of Uterus

The lower cylindrical part (3 cm) protruding into the vagina. Its junction e' uterus = int. os. & its opening into the vagina = ext. os. Has narrow lumen (1 cm) formed of:

### 1. Mucosa:

#### a. Endocervix [cervical canal]:

lined e' s. col. mucus secreting cells + lamina propria containing cervical glands (branched tubuloalveolar mucus secreting) lined e' s. col.

b. Ectocervix: the outer surface & ext. os are lined e' non. Kerat. str. sq. Cervical mucosa do not show cyclic changes during the menstrual cycle (i.e. do not shed)

### 2 Stroma:

= dense fibrous c.t. e' few smooth ms., so cervix is firm & rubbery.

During labor, under control of relaxin hr. from the placenta, Cervix becomes soft & dilated due to separation of the parallel collagen bundles w become irregular [collagenolysis].

Collagenolysis: during labor, M conc<sup>n</sup> of hyaluronic A. withdraw H<sub>2</sub>O bet. collagen fs. → their separation → cervical dilatation (to reach 10 cm) to pass fetal head

### Cervical Mucus:

- plays an imp. role in fertilization.
- During proliferative phase & time of ovulation, cervical mucous is abundant, thin & watery → easy movement of sperms to uterus & fertilize the ovum.
- After ovulation (in secretory phase) or if pregnancy occurs, cervical mucous becomes viscid & scanty to prevent entrance of sperms or bacteria to the uterus.

Smears of cervical epith. are imp. for early diagnosis of cervical Carcinoma

## Menstrual Cycle

= Cyclic changes in the endometrium. Starts at puberty [12-15 years] until the age of 45-50 years [= fertile period of ♀]. Under control of FSH & LH of pit. & ovarian hormones [estrogen & progesterone]. Its duration is about 28 days. 3 phases:

### 1. Menstrual (destructive) phase:

- From 1<sup>st</sup> to 5<sup>th</sup> day.

If no fertilization occurs, C.L. stops functioning 10-12 days after ovulation → sudden drop of bl. estrogen & progesterone → vasoconstriction of spiral arteries → ischemia & necrosis & shedding of the functional zone

While the basal zone (0.5 mm) remains from w regeneration starts. the capillaries rupture → bleeding



## [2] - Proliferative phase : [follicular - estrogenic phase]

- from 5<sup>th</sup> to 14<sup>th</sup> day
- under control of pituitary FSH & ovarian estrogen.
- estrogen stimulates proliferation & regeneration of the basal zone (2.5 mm)
- endometrial epith. (s.col. part.cil) regenerates.
- endometrial glands regenerate : become narrow & straight but no secretory function.

## [3] Secretory phase : [luteal - progestational phase]

- from 14<sup>th</sup> day till onset of next bleeding.
  - under control of pit. LH & ovarian progesterone
  - endomet. ↑↑ in thickness (5 mm).
  - endomet. glands : become tall, tortuous, dilated & cells accumulate glycogen in their basal parts, later on glycogen reach the apex of the cells & the lumen of the gland is full of secretion.
  - Spiral arteries : dilated ; tortuous & congested.
  - Stroma : become edematous, fibroblasts ↑ in No & size (rich in <sup>mit</sup> GA) & called decidual cells. <sub>FER</sub>
- These changes are called decidual reaction.

### Decidual cells:

1. Secrete prostaglandins: stimulate uterine contract<sup>n</sup> during labor.
2. " Prolactin : \* regulate amniotic fluid vol. & fetal H<sub>2</sub>O balance.  
\* has paracrine control → ↑↑ secretion of the endometrial gls. in 1<sup>st</sup> trimester.  
\* affect synthesis of fetal surfactant.  
\* " Ca<sup>++</sup> absorption in fetal gut.

The high level of progesterone in " secretory phase inhibits contract<sup>n</sup> of sm.ms of myometrium not to interfere w<sup>th</sup> implantation of the embryo

After Fertilization, the embryo reaches the ut. (day 5-6 after ovulation)  
its main source of nutrition is the secretion of the endometrial glands.



# Placenta

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def. Temporary endocrine gland & the site of exchanges bet. the mother & foetus.

Formed of:

## A. Maternal Part = [Decidua Basalis]

the fibroblasts in endometrial c.t. enlarge & show features of ptn. forming cells & now called decidual cells. The thickened endometrium is called decidua.

Decidua is divided into: decidua basalis: bet. embryo & myometrium.

decidua capsularis: bet. the embryo & uterine cavity.

decidua parietalis: endometrium lining the rest of the uterine cavity.

Decidua basalis is the most imp part that forms the placenta.

## B. Fetal Part = [Chorioic Villi]

= Finger like projections from the blastocyst. They branch & anastomose & become embedded in the decidua basalis, separated by intervillous spaces containing maternal blood. Each chorionic villus is formed of:

1. Central core of foetal c.t. containing foetal bl. vs & macrophages = Hofbauer Cells

2. Trophoblast: epith. cover: 2 layers:

a. Inner Cytotrophoblast: 1 layer of cuboidal cells & pale cytoplasm

It disappears by the end of 4<sup>th</sup> month of pregnancy

b. Outer Syncytiotrophoblast: 1 layer of dark cells & no cell boundaries so appear as multinucleated layer. Has microvilli w invade the decidua basalis.

## Placental Barrier:

The wall w separates blood in fetal circulation from bl. in maternal circulation.

Formed of:

1. endothelium of foetal capillary.

2. basement memb. of foetal capillary.

3. Foetal c.t. containing Hofbauer cells.

4. Basement memb. of trophoblast.

5. Trophoblast: cytotrophoblast & syncytiotrophoblast in the 1<sup>st</sup> 4 months (syncytiotrophoblast only in the last 5 months).

## Functions of Placenta:

1. passage of O<sub>2</sub>, nutrients, hormones, antibodies from mother to fetus.

2. remove CO<sub>2</sub> & waste products.

3. Endocrine function: Syncytiotrophoblast secretes:

a. Human chorionic gonadotropin: maintain corpus luteum of pregnancy after LH of pit. stops.

b. Human chorionic somatomammotropin: lactogenic & growth stimulating

c. Estrogen & progesterone.

d. Chorionic thyrotropin (similar to TSH)

e. " " Corticotropin ( " " ACTH)

f. relaxin: softening & dilatation of cervix during labor.



#### 4. Placental Barrier Functions:

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- protect the embryo from harmful bacteria.
- allow passage of maternal Ig to fetal bl. to passively immunize the fetus against bacteria.

#### Placenta Previa:

The placenta implants in the lower part of uterus close to the int. os.  
The main cause of 3<sup>rd</sup> trimester bleeding. Usually necessitates emergency Cesarean section.

#### Vagina

Fibromuscular tube 7-9 cm long. Formed of:

##### (1) Mucosa:

###### (a) Non-Keratinized St. sq. epith.:

- estrogen stimulate cells to form & accumulate glycogen.
- As vaginal cells desquamate, glycogen deposit in the lumen.
- glycogen by Vaginal bact. lactic acid → acidic PH to protect against harmful bact. & fungi.  
Lactobacilli

###### (b) Lamina propria: loose c.t. rich in elastic fs.

##### (2) Musculosa: Inn. circ. & Out. long. sm. ms.

##### (3) Adventitia: dense c.t. rich in elastic fibres.

The mucus found in the vagina comes from the cervical glands as the vagina has no glands.

The great elasticity of vagina (large N<sup>o</sup> of elastic fs in lamina propria & adventitia) allows temporary distention during labor.

#### The external Genitalia

Labia Majora = 2 folds of fatty skin & sm. ms. The inner surface has no hairs while the outer surface is covered e' hairy skin e' sweat & sebaceous glands.

Labia Minora = 2 folds of skin e' a core of loose c.t. rich in elastic fs. The outer & inner surfaces have sweat & sebaceous gls. but no hairs & no fat.

Clitoris = erectile tissue = 2 corpora cavernosa covered e' thin skin e' no hairs, no sweat or sebaceous glands.

Hymen: perforated memb. at the lower end of vagina = c.t. core covered on both sides by st. sq. epith. = the junction bet. ext. & int. genitalia.

Bartholin's gls: mucous glands on either side of the vestibule

\* Vestibulum = the space bet. the 2 labia minora.

Ext. genitalia esp. clitoris are rich in sensory n. endings e.g. Meissner's &



# The Mammary Gland

• def. : Exocrine, compound alveolar, apocrine gland.

## • Structure & development:

At birth = nipple, surrounding areola + duct system in dense c.t.

After puberty : breast enlarges due to  
(under control of estrogen) → accumulation of fat  
→ branching of ducts.

## 1. In Resting State:

The nipple = raised area of dense c.t. rich in smooth muscles covered e' pigmented skin, rich in sensory ns, & contain opening of 12-20 lactiferous ducts.

Areola : pigmented skin around the nipple e' modified sebaceous glands (Montgomery gls.).

### Parenchyma:

12-20 lobes separated by thick c.t. septa rich in fat cells. Each lobe contains branching lactiferous ducts lined e' cuboidal cells, surrounded by myoepith. cells & embedded in abundant loose c.t. Small ducts empty into a large lactiferous duct that dilates → lactiferous sinus (lined e' stratified cuboidal epith.) that changes into str. sq. epith. at it's external opening in the nipple.

## 2. In Pregnancy & Lactating State:

Under control of estrogen, progesterone, prolactin, chorionic somatomammotropin the following changes occur:

- The breast enlarge in size.
- The nipple & areola become more pigmented (rarely returns to normal color).
- Montgomery gls. enlarge.
- Alveoli proliferate at the end of the ducts.
- Alveoli are lined e' s.col. + myoepith. cells. Col. cells secrete milk, so, rich in mit., rER, G.A. (ptn) + s-ER, fat droplets (lipids).
- Milk is rich in ptns. (1.5%), lipids (4%), lactose (7%) + the apical parts of cytoplasm (apocrine).
- It appears acidophilic & vacuolated due to dissolved fat.
- The C.T. septa become thinner & fat cells ↓↓.
- The amount of loose c.t. ↓↓.



### 3. Post-lactation changes :

After weaning, most alveoli degenerate & dead cells are removed by macrophages & breast returns to resting state.

### 4. Post-menopausal changes :

↓↓ estrogen → atrophy & reduced size.

Clostrum = the 1<sup>st</sup> secretion after labour & less fat, more ptn. & rich in Abs (Ig A) for passive immunity of the newborn.

### Hormonal Control of the breast:

Estrogen : enlarges the breast at puberty → accumulation of fat & branching of the ducts

Estrogen, progesterone + chorionic somatomammotropin : at pregnancy  
→ enlarged breast & more branching of ducts & development of alveoli.

Prolactin → milk secretion during lactation

Oxytocin → milk ejection by contraction of myoepith. cells

### ♂ Breast :

= small amount of fibrous c.t. + rudimentary duct system.

It may enlarge at puberty due to accumulation of fat.

This enlargement is mild, self limited & reversible.

### Breast Cancer : [in females]

- The first in Egypt & all arabian countries mainly in lactiferous ducts.  
If malignant cells metastasize to lungs, liver, brain & bone maybe fatal.
- Early detection [by self examination, mammography & ultrasonography]  
followed by early treatment → better prognosis & ↓↓ mortality.



# Urinary System

## Kidneys

def. compound tubular gland responsible for:

1. Excretion of urine & its waste products. (urea & uric A)
2. Regulate fluid & electrolyte balance + reabsorption of  $H_2O$ .
3. production of: renin, erythropoietin & medullipin I

**Formed of:**

### I Stroma:

- a. capsule: dense fibrous c.t. Thin, covered & adipose c.t.
- b. renal interstitium: contains fibroblasts, macrophages + Interstitial cells  
 & secrete **Medullipin I** converted in the liver into **Medullipin II** (potent hypotens)

### II. Parenchyma:

#### A. Cortex

\* red (rich in bl. vs.) & granular (renal corpuscles) \* Formed of:

Malpighian renal corpuscles, convoluted tubules, medullary rays + peritubular vs.

\* It includes:

1. Cortex proper: under the capsule.
2. Columns of Bertini: between the medullary pyramids (on either side)
3. Cortical labyrinth: surround the medullary rays = nephrons that drain into the same collecting tubule

#### B. Medulla:

\* grey \* 6-12 medullary pyramids. The base of the pyramid points to the Cortex & its apex (renal papilla) points to the renal pelvis. It is perforated by 20 openings of collecting ducts = ducts of Bellini.

The apex projects into a minor calyx. 3-4 minor calyces → a major calyx → empty in renal pelvis [the upper expanded end of the ureter].

\* Each pyramid shows radial striations [Collecting tubules, ducts of Bellini vasa rectae + straight tubules of loop of Henle.] = Medullary rays

\* The medullary rays extend into the cortex.

• **Renal Lobe** = medullary pyramid + overlying cortical arch + Columns of Bertini on either side of the pyramid.

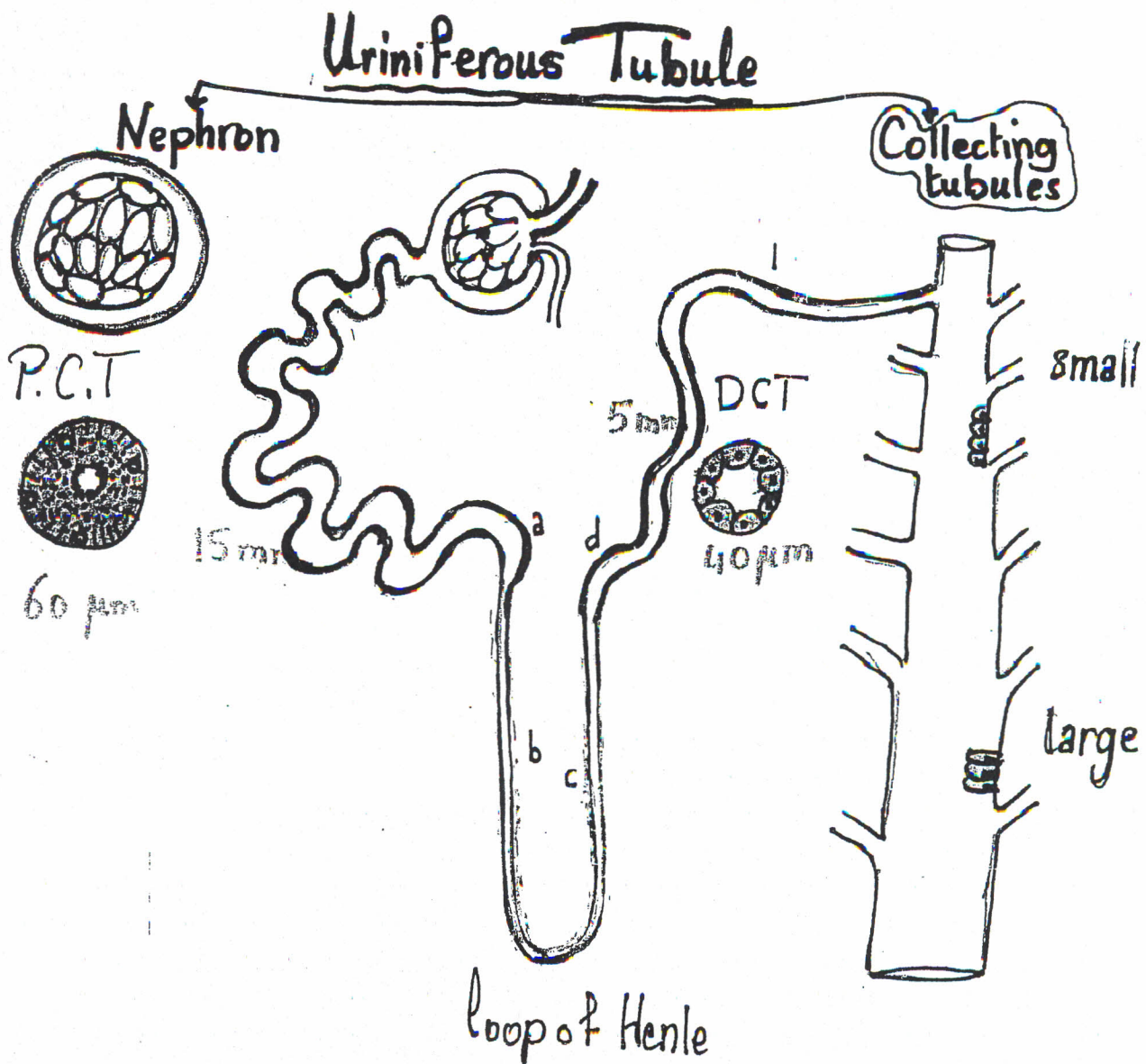
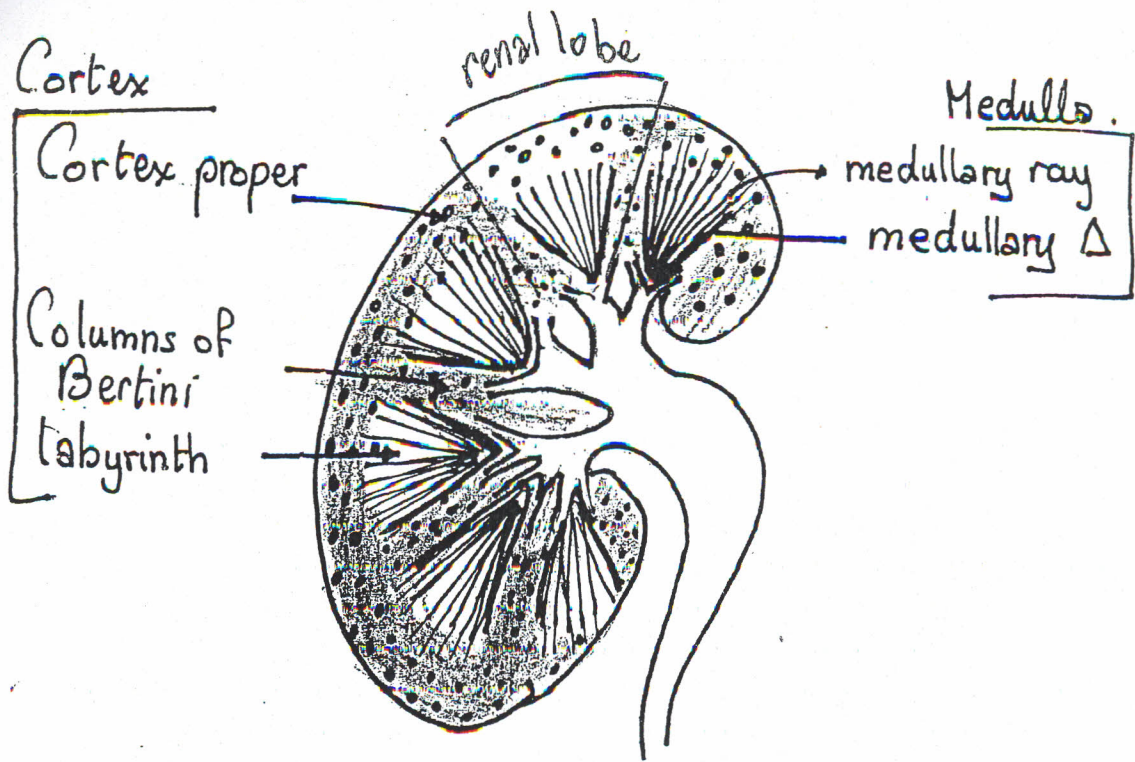
• **Renal Lobule** = Each medullary ray = collecting duct & all nephrons that it drains. Demarcated by interlobular arteries.

### The Uriniferous Tubule

Nephron

Collecting duct







## A. The Nephron.

- The structural & functional unit of the kidney.
- each kidney contains 1-1.4 million nephrons.
- Each nephron is formed of
  - ↳ Malpighian renal corpuscle
  - ↳ proximal & distal convoluted tubules.
  - ↳ loop of Henle.
- Classified into:
  - a. Cortical nephrons: e' short loop of Henle.
  - b. Juxta-medullary nephrons: e' long loop of Henle.

### 1. Malpighian Renal Corpuscle:

- about 200  $\mu\text{m}$  in diameter. Formed by invagination of the spherical blind end by a tuft of capillaries [Glomerulus]  $\rightarrow$  Bowman's capsule.
- Has 2 poles:
  - a. Vascular pole: where an afferent arteriole enters & efferent arteriole leaves.
  - b. Urinary pole: continuous e' the proximal convoluted tubule.
- Each renal corpuscle is formed of glomerulus & Bowman's capsule.

### Glomerulus

- At the vascular pole, afferent arteriole [carrying unfiltered blood] divides repeatedly  $\rightarrow$  capillary tuft  $\rightarrow$  drain into efferent arteriole [carry filtered blood]. - The afferent arteriole have larger diameter & thicker media than the efferent arteriole [to create high glomerular press. to produce large amount of glomerular filtrate].

L.M. - lined e' fenestrated endothelium

- the basement membrane is: thick & continuous. (PAS+ve).

E.M. - The endothelium has pores (100 nm in diameter) Not covered by diaphragms.

- The Glomerular Basement membrane (GBM) =

- Formed of 3 layers:
  - a. lamina rara [lucida] externa = out. electron lucent
  - b. lamina rara [lucida] interna = inner " " "
  - c. lamina densa = central electron dense L.

### Bowman's Capsule

- A double wall cup-shaped epith. capsule. Formed of 2 continuous layers:
- Formed of 2 layers:
  - a. Outer parietal layer: lined e' simple squamous epith.
  - b. Inner Visceral layer: Invests the glomerular capillaries, formed of, modified squamous cells called podocytes.
- The visceral & parietal layers are separated by capsular space.



## Podocyte :

def. = modified squamous cells lining the visceral layer of Bowman's capsule.

E.M. = stellate shaped cells separated from the glomerular capillaries by subpodocytic space. Have cell body from w major processes arise. From major processes, minor processes arise & are implanted at intervals on the glomerular capillaries. The minor processes of adjcent podocytes interdigitate leaving gaps bet. them. The gaps are called filtration slits, covered by semipermeable memb. called [filtration slit diaphragms].

The filtration slit diaphragms = trans memb. protein nephrin  
→ Zipper - like sheet. It has central dense core & pores on both sides.

The cytoplasm contains many ribosomes, r.ER, mit., Golgi complex & actin microfilaments (podocytes are contractile)

### Functions :

1. Involved in formation of the blood renal barrier.
2. renewal of the basement membrane of glomerular capillaries.

## The Blood Renal Barrier : Glomerular Filtration Barrier

It is the barrier w separates blood in the glomerular capillaries from the glomerular filtrate in the capsular space & through w filtration of blood occurs. Formed of :

### ① Fenestrated endothelium of the glom. capillaries :

depends on molecular weight & size. It allows passage of molecules smaller than bl. cells & platelets e.g. plasma proteins

### ② Glomerular basement memb. [GBM]

- the most effective barrier. the only continuous layer. depends on :

#### a. Molecular weight :

- prevent passage of large molecules ( $> 160,000$  Dalton) e.g. plasma ptns
- allows " " small " e.g. sugars & a.a.s.

#### b. Molecular charges :

The -ve charges on both laminae rarae prevent passage of -ve charged molecules e.g. albumin (although its MW is 69,000 Dalton)

### ③ Filtration Slit diaphragms :

- Cover the spits bet. the feet of podocytes & depends on :

#### a. Molecular weight : allows passage of molecules e' MW $< 40,000$ D

b. Molecular charges : It is -vely charged so, prevent passage of -vely charged molecules.



## The Mesangial Cells:

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- Shape:** small stellate cells. Have small dark nuclei. Basophilic cytoplasm rich in lysosomes.
- Types & sites:**
  - (a) Intraglomerular: bet. the glomerular capillaries in the renal corpuscle
  - (b) Extraglomerular: at the vascular pole.
- Functions:**
  - Supportive function:** secrete collagen, chondroitin sulphate, fibronectin & mesangial matrix.
  - renewal of GBM.**
  - Contractile function:** so, regulate bl. flow in glom. caps. in response to vaso-active subs.
  - Phagocytic "** : extend processes bet. endoth. cells of glom. caps to phagocytose debris or residues during renewal of GBM
  - Extra glom. mesangial cells:** form part of Juxtaglom. apparatus.

|                              | <u>[2] Proximal Convoluted tubule</u>                                                                                                                                                                                                                                                                                                                                                                         | <u>[3] Distal Convoluted tubule</u>                                                                                                                                                                                                                                                                                                     |
|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Size</b>                  | <ul style="list-style-type: none"> <li>- longer (15 mm).</li> <li>- more convoluted.</li> <li>- larger diameter (60 <math>\mu</math>m).</li> <li>- narrow lumen.</li> </ul>                                                                                                                                                                                                                                   | <ul style="list-style-type: none"> <li>- shorter (5 mm)</li> <li>- less convoluted.</li> <li>- small diameter (40 <math>\mu</math>m)</li> <li>- wider lumen.</li> </ul>                                                                                                                                                                 |
| <b>Site</b>                  | <ul style="list-style-type: none"> <li>- starts at urinary pole of renal corp</li> <li>- ends at descending limb of loop of Henle</li> </ul>                                                                                                                                                                                                                                                                  | <ul style="list-style-type: none"> <li>- start at end of ascending limb of loop of Henle</li> <li>- ends at collecting duct.</li> </ul>                                                                                                                                                                                                 |
| <b>L.M. of lining epith.</b> | <ul style="list-style-type: none"> <li>- 3-4 cells</li> <li>- high cuboidal (<math>\Delta</math>) cells</li> <li>* non-clear boundaries.</li> <li>- Apical brush border.</li> <li>• basal acidophilic striations.</li> <li>- deeply acidophilic &amp; granular cytoplasm</li> <li>- rounded &amp; basal nuclei</li> </ul>                                                                                     | <ul style="list-style-type: none"> <li>- 5-8 cells (up to 20 in macula densa)</li> <li>- low cubical cells.</li> <li>* clear boundaries.</li> <li>- less brush border.</li> <li>• Less basal striations.</li> <li>- Less acidophilic &amp; less granular.</li> <li>- rounded &amp; central nuclei.</li> </ul>                           |
| <b>E.M.</b>                  | <ul style="list-style-type: none"> <li>- apical long microvilli <math>\rightarrow</math> brush border</li> <li>* extensive interdigitations of lat. membrane <math>\rightarrow</math> non-clear boundaries</li> <li>• Basal infoldings &amp; associated parallel mitochondria <math>\rightarrow</math> basal striations</li> <li>- numerous mitochondria <math>\rightarrow</math> more acidophilic</li> </ul> | <ul style="list-style-type: none"> <li>- Fewer &amp; shorter microvilli <math>\rightarrow</math> no brush border</li> <li>* Less interdigitations <math>\rightarrow</math> clear boundaries</li> <li>• present but less <math>\rightarrow</math> less</li> <li>- less mitochondria <math>\rightarrow</math> less acidophilic</li> </ul> |
| <b>Functions</b>             | <ul style="list-style-type: none"> <li>- reabsorption of glucose &amp; a.a.</li> <li>- reabsorption of <math>\text{Na}^+</math>, <math>\text{Cl}^-</math>, <math>\text{K}^+</math> &amp; <math>\text{H}_2\text{O}</math>.</li> </ul>                                                                                                                                                                          | <ul style="list-style-type: none"> <li>- reabsorption of <math>\text{Na}^+</math> &amp; <math>\text{H}_2\text{O}</math> under control of aldosterone &amp; ADH</li> <li>- excretion of <math>\text{H}_2</math> &amp; <math>\text{NH}_3</math></li> </ul>                                                                                |

**In Diabetic nephropathy & Glomerulonephritis:** the glomeruli are affected & the barrier is disrupted  $\rightarrow$  albuminuria or hematuria



## 4. Loop of Henle

- U-shaped tube connects the PCT & DCT.
- present in medullary rays in cortex & medulla.
- Cortical nephrons have short loop of Henle while Juxtamedullary " " long " " " " " " .
- Formed of:
  - Thick descending part: similar to PCT, lined e' cuboidal epith.
  - thin " limb: lined e' simple squamous epith.
  - " ascending " " " " " " " "
  - thick " part: similar to DCT, lined e' s. cubical epith.

### Functions:

Conc<sup>n</sup> of Urine (Hypertonic urine) & conserving H<sub>2</sub>O.

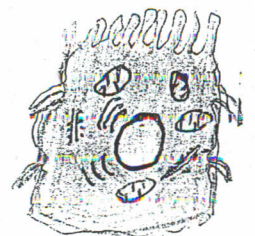
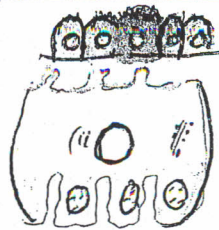
## B. The Collecting Tubules

- The excretory part of the uriniferous tubules.
- a group of nephrons drain into <sup>arched</sup> collecting tubule (lined e' s. cuboidal)
- Each 6-8 small collecting tubules drain into straight collecting duct = duct of Bellini (lined e' s. col. epith.) w open into the tips of the medullary pyramids

Function: Conc<sup>n</sup> of urine under control of ADH

The collecting tubules & ducts have 2 types of cells:

|                                   | Principal cells               | Intercalated cells            |
|-----------------------------------|-------------------------------|-------------------------------|
| <b>No</b>                         | - numerous.                   | - Few                         |
| <b>Stain Intensity</b>            | - Weak (pale)                 | - dark                        |
| <b>EM:</b>                        |                               |                               |
| • Organelles                      | - Few                         | - Abundant.                   |
| • mitochondria                    | - Few, small, spherical       | - more                        |
| • Basal infoldings                | - numerous (ion transporting) | - absent                      |
| • microvilli                      | - short & scanty.             | - more                        |
| • lat. interdigitat <sup>ns</sup> | - Absent (clear boundaries)   | - More (non-clear boundaries) |



**Diabetes Insipidus:** insufficient product<sup>n</sup> of ADH →  
 ↓ reabsorption of H<sub>2</sub>O from the collecting tubules →  
 hypotonic pale ~~urinated~~ urine but normal bl. sugar.



# Juxta. Glomerular Apparatus

-7-

def.: complex structure at the vascular pole of some renal corpuscles  
formed of:

## 1. Juxta. glomerular cells: (J.G. cells)

modified smooth muscles of the tunica media of the afferent (sometimes efferent) arteriole. Shows the following changes:

- 1. nuclei become rounded. 2. Cytoplasm have PAS+ve secretory granules (renin)

Function: secrete renin enz.

## 2. Macula densa:

= The part of the DCT that fits bet. the afferent & efferent arterioles at the vascular pole. It shows the following changes:

- Cells ↑ in No. & height (become columnar) & their nuclei become apical, dark & closely packed so appear as dark spot by the L.M.
- G.A. becomes infranuclear (basal).
- The basement memb. is absent so, cells become in contact w/ J.G. cells.

Function: Osmoreceptors. it monitors the level of  $\text{Na}^+$  in the DCT.

## 3. Extra glomerular Mesangial cells:

[Lacis cells, Polkissen cells in Polar Cushion]

pale cells in between the afferent, efferent arterioles & macula densa.

Function: supportive & may transmit signals from macula densa to glom. cap

## • Functions of J. G. Apparatus:

regulates bl. press. through Renin. Angiotensin - aldosterone system:

1. drop of bl. press. or vol. (as in hemorrhage) → ↓↓ vol. of glom. filtrate
2. ↓↓  $\text{Na}^+$  &  $\text{Cl}^-$  ion conc<sup>n</sup> in DCT.

3. Macula densa monitors the changes & stimulate J.G.C → renin

4. Angiotensinogen  $\xrightarrow{\text{renin}}$  Angiotensin I  $\xrightarrow{\text{ACE}}$  Angiotensin II  
(in bl. & formed in liver)

ACE = angiotensin converting enz. secreted by endoth. of lung caps

5. Angiotensin II raises bl. press. by:

vasoconstriction

stimulate Adr. cortex

stim. pit. gl  
↓ release

Aldosterone

ADH

↑↑  $\text{Na}^+$  reabsorption in DCT

↑↑  $\text{H}_2\text{O}$  reabsorpt<sup>n</sup> in collecting tubules

Return of bl. press.  $\xrightarrow{\text{-ve feedback}}$  inhibits secretion of renin by J.G. A.



## Blood Supply of Kidney

Renal artery: at the hilum gives:

Interlobar arteries: between the pyramids. At the cortico-medullary junction it gives Arcuate arteries at the base of the pyramids.

It gives Interlobular arteries: that terminate as capsular capillaries

Interlobular arterioles: give many afferent arterioles → glomerular capillaries → efferent arterioles that give peritubular capillaries (supply the PCT & DCT) → peritubular venules → interlobular vein → arcuate vein → inter-lobar vein → renal vein at the hilum.

• Juxta-medullary efferent arterioles → straight arteriolae rectae w extend in the medullary pyramids → venulae rectae w drain into interlobular or arcuate vein → renal v.

∴ Vasa rectae =

## Urinary Passages

minor & major calyces → renal pelvis → Ureter → Urinary bl. → Urethra.

### Ureter

It's wall is formed of:

#### I. Mucosa:

shows longitudinal folds  
→ stellate shape lumen.

- = (a) transitional epith
- (b) underlying c.t. corium

Both, the folds & the epith. allow distention of the ureter to allow passage of small stones in urine

#### II. Musculosa:

The upper  $\frac{2}{3}$ : inner long. & outer circ. The lower  $\frac{1}{3}$  has additional outer long. L.

Their contraction → peristaltic wave so propel urine → Ur. bladder.

#### III. Adventitia:

fibro-elastic c.t. rich in bl. vs. nerves L. vs.

### Urinary bladder

It's wall is formed of:

#### I. Mucosa:

(a) Transitional epithelium:

In empty bladder 5-6 layers & superficial cells are cuboidal & bulge in the lumen (dome or umbrella cells)

In full bladder: 3-4 layers & superficial cells become squamous.

(b) Underlying c.t. corium.

#### II. Musculosa:

formed of inner & outer long. & middle circular sm. ms.

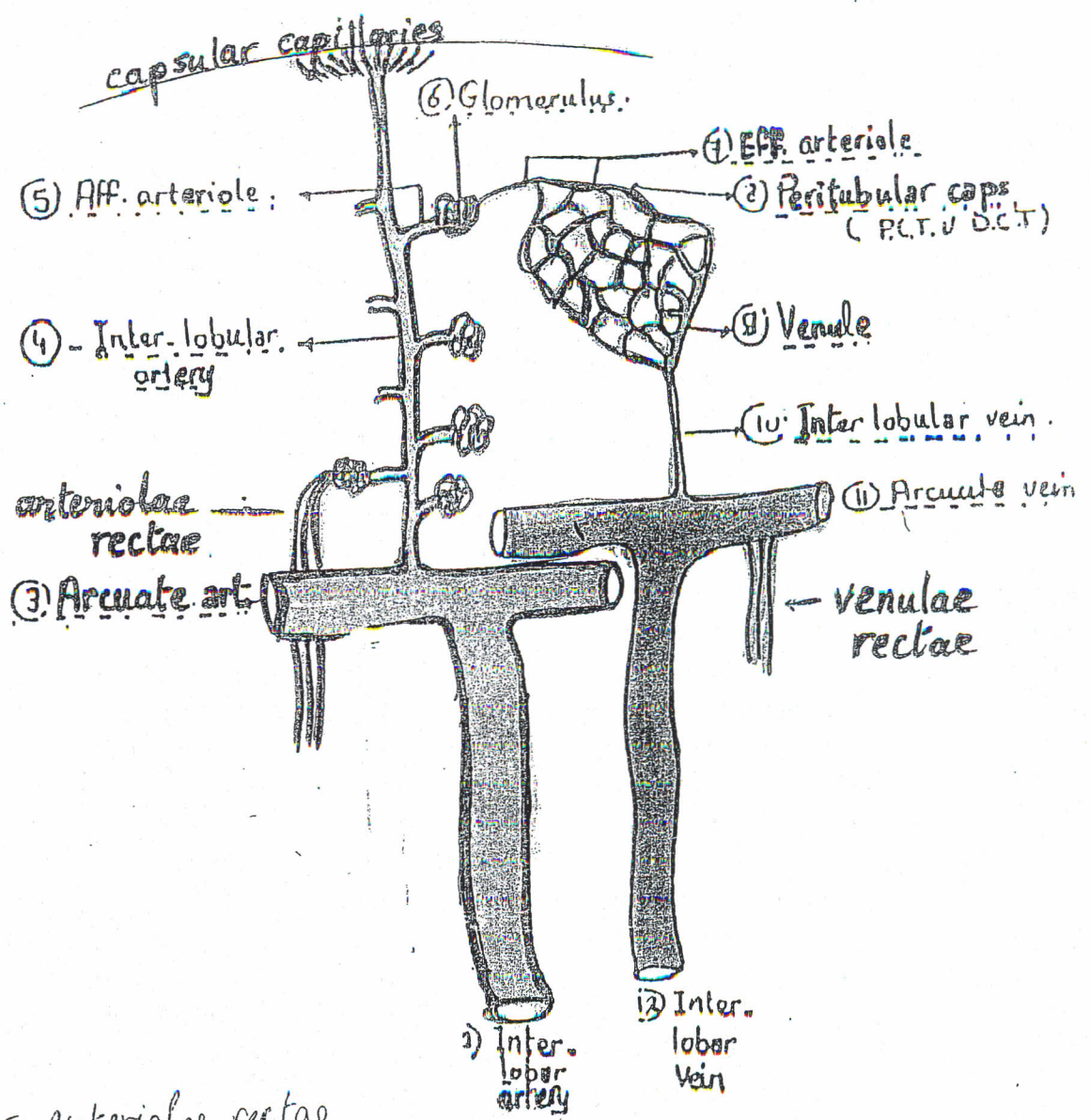
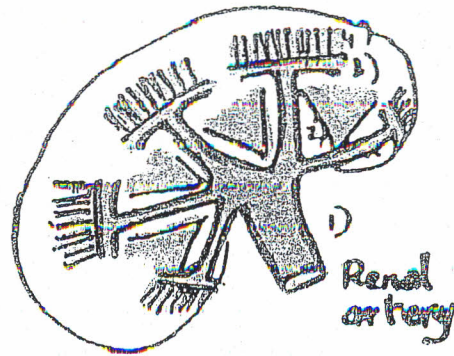
At the neck of the bladder, the inn. long. becomes circ. to form the internal urethral sphincter.

#### III. Adventitia:

fibro-elastic c.t. except the sup. part, covered e' serosa



# Blood Supply of the Kidney



Cortex

Medulla

Vasa rectae = arteriola rectae + Venulae



Uro epith. = Transitional epith. ∴ 3 layers :

1. Basal layer : 1 layer of cuboidal cell resting on non clear b.m.
2. Intermediate L. : several layers of polyhedral cells.
3. Superficial "umbrella cells" L. : dome shaped cells, may be binucleated

## Urethra

### ♂ Urethra :

20 cm long tube that carries both urine & semen. Divided into

#### 1. Prostatic Urethra :

- passes through the prostate
- lined e' transitional epith.
- surrounded by the int. urethral sphincter

#### 2. Membranous Urethra :

- passes through the urogenital diaphragm.
- lined e' pseudo-stratified col. epith. or st. col.
- surrounded by skeletal ms. of pelvis → ext. sphincter.

#### 3. Penile Urethra :

- passes in corpus spongiosum of the penis.
- lined e' stratified columnar epith. w changes into st. sq. at it's terminal part (fossa navicularis)
- Glands of Littre open into it.

### ♀ Urethra :

a short tube lined e' transitional, ps. st. col or st. col. then st. sq. at it terminal end.

Urinary Incontinence = loss of voluntary control on the ext. urethral sphincter ms. esp. in older women



# The Eye

-1-

## A. Outer Fibrous (Supporting) Layer:

### ① Cornea ( $\frac{1}{6}$ of fibrous coat): (5-layers).

#### 1. Non-Keratinized stratified sq. epith. (5-6 Ls.)

② Basal Layer = cub. or col. cell resting on a straight b.m. They show mitotic figures (high regenerative power) as long as the b.m. is intact.

③ Intermediate Layer = 3-4 Ls of polyhedral cells & free unmyelinated nerve endings (for protection)

- The superficial L. = flat cells & microvilli to retain a film of tears to keep it wet.

### 2. Bowman's memb. = [Ant. limiting memb.]

= the b.m. of the epith. • Thick  $\rightarrow$  strength & stability.

• Non-cellular = collagen fibrils • protect against infection

• Cannot regenerate, if injured  $\rightarrow$  corneal opacity.

### 3. Substantia propria:

about 60 parallel collagen bundles separated by fibroblast like cells = Keratocytes in rows embedded in ground substance rich in proteoglycans [lumican] to maintain their arrangement.

### 4. Descemet's memb.:

- represent the b.m. of the corneal endoth.

- Non-cellular = fine interwoven collagen fibres.

### 5. Endothelium := s. sq. endoth.

Functions: 1. maintain Descemet's memb.

2. pump  $\text{Na}^+$  into the ant. chamber passively followed by  $\text{Cl}^-$  &  $\text{H}_2\text{O}$

This keeps optimum state of corneal hydration for maximal transparency.

## Factors Causing Corneal transparency:

1. It is avascular.

2. Regular arrangement of collagen lamellae.

3. The lamellae, cells & matrix have the same refractive index.

4. The epith. is non-keratinized.

5. minimal hydration of cornea.

6. Unmyelinated free nerve endings.

\* Lasik surgery: Laser can change corneal curvature to correct vision.

\* Microvilli (film of tears) keep the cornea wet to avoid ulceration.

\* Injury of the ant. limiting memb. [Bowman's memb.]  $\rightarrow$  corneal opacity.

\* Corneal transplantation is usually successful (avascular)



## [2] - Sclera: (post 5/6 of the Fibrous coat)

Opaque, formed of type I collagen bundles in various directions + fibroblasts + elastic fs. Extraocular ms are inserted in its ant. part. Relatively avascular.

### Changes at the Corneo-scleral junct? [Limbus]

1. Conjunctival epith. = non-kerat. st. sq. epith. Stem cells of stratified epith are concentrated at the limbus.
2. Bowman's memb is replaced by subconj. c.t.
3. The collagen bundles become irregular e' appearance of canal of Schlemm.
4. microvasculature of the cornea appear at the limbus.
5. Descemet's memb. & endothelium are replaced by trabecular meshwork e' channels lined e' irregular endoth. they drain aqueous humor from the ant. chamber to canal of Schlemm.

## Refractive Media of Eye

= the transparent media through w light passes to reach the retina.

### [1] - The Cornea:

### [2] - Aqueous humor:

- transparent fluid in the ant. & post. chambers.
- Similar to plasma [in its inorganic ionic content] but e' less total ptn. (0.1%)
- Secreted by: the inner L. of epith. covering the ciliary processes.
- Circulation: passes from the post. chamber through the pupil to the ant. chamber  
→ iridocorneal angle → spaces of Fontana → Canal of Schlemm → scleral v/s

**Glaucoma** = ↑ intraocular press. due to impaired drainage of aqueous humor. If not treated → press on optic n. fs → degenerat<sup>n</sup>, gradual loss of vision.

## [3] Vitreous body:

= transparent mucoid c.t.

- present behind the lens in the vitreous chamber.
  - Contains Vitreous humor = 99% H<sub>2</sub>O + hyaluronate & small amount of collagen type IV + cells
  - The only cells present are macrophages + hyalocytes → form Hyaluronate + collagen
- Funct<sup>n</sup>: supports the lens anteriorly & the retina posteriorly.



## 4. Lens:

- 3 -

Avascular & transparent structure. Ciliary Zonule is inserted in its capsule to join it to the ciliary body. Formed of:

a. Lens Capsule: thick, homogenous, rich in collagen (type IV) + proteoglycans  
Covers the lens & support lens epith.

b. Subcapsular epith: 1 layer of cuboidal cells only on the ant. surface of lens. Cells at lens equator divide to allow growth of lens (periphery)

c. Lens Fibres := elongated cell that develop from stem cells in lens epith. w lose their organelles & nuclei & become filled w ptn Crystall. specialized for light refraction.

Cataract = loss of lens transparency due to denaturation of crystallins.

Presbiopia = " " " elasticity in old age → loss of accomodat<sup>n</sup> for near vision.

## B. The Middle (Vascular) layer

### 1. The Iris

def.: the ant. part of vascular layer perforated at the centre by the pupil.

- It's ant. surface: irregular non-continuous L. of packed fibroblasts & melanocytes & interdigitating processes.

- It's post. surface: covered w 2 layers of pigmented epith. continuous w that on the ciliary processes.

- Stroma: loose vascular pigmented c.t. w contains → Constrictor pupillae & dilator " ms.

\* Functions: 1. Controls pupil size & amount of light.  
2. blocks entrance of light (abundant pigment) except at pupil  
3. give color of eye.

Albinism: The iris has no pigments. It's pink color is due to light reflected from stromal bl. vs.

### 2. The Ciliary body

= Vascular c.t. contains pigment cells + Ciliary muscles + elastic fibres.

• Ciliary epith = 2 layers of low col. cells:

[ Out. layer: (towards c.t.) is pigmented.  
Inn. " : ( " surface) " non- " ]

• Ciliary muscles: sm. ms inserted on the sclera. The arrangement of the fibres → reduces the size of the ciliary body on contract<sup>n</sup>. → tension on the zonule.



• Ciliary processes: finger like projections from the med. side of ciliary body covered e' ciliary epith. & contains capillary loops from w aqueous humor is secreted.

Functions: (1) Form aqueous humor. [by the non pigmented L on the processes]  
(2) Accomodation for near vision (ciliary ms.)

### 3. The Choroid

lies bet. retina & sclera: Formed of:

(a) Suprachoroid lamina [SCL]:

= c.t rich in pigment cells + fibroblasts + elastic fs.

(b) Choroido capillaries = fenestrated capillaries to nourish the out. part of the retina.

(d) Bruch's membrane: Acellular memb. = 5 layers

- a middle layer of elastic fs e' collagen fs on either side.

- The outermost layer = the b.m. of the choriocapillaries.

- " inner " " = " " " pigmented cells of retina.

F - It act as a retinal barrier to limit entrance of microbes from the fenestrated capillaries of choriocaps. to the outer part of retina.

### The Inner Nervous Layer [Retina]

have 3 types of cells

↓  
Neurons

↓  
Neuroglial cells

↓  
pigment cells.

Formed of 10 layers:

#### ① Pigment Cell Layer:

Single layer of low cot. cells e' basal rounded nuclei resting on Bruch's memb.

- The inner part: contains melanin pigment.

EM have basal mit. rER, s.ER, lysosomes

- " apical microvilli w interdigitate e' rods & cones

- The lat. walls are joined by Z. occludens, Z. adherens, desmosomes & gap J.

Functions:

1. share in formation of Bruch's memb.

2. Melanin absorbs extra light to prevent reflections w

3. phagocytose old discs shed by rods

4. estrification of vit. A (by s-ER) to regenerate retinoids

5. Form bl. retinal barrier.

In Retinal Detachment: the pigmented epith. is firmly attached to Bruch's memb. & the choroid, while the other nine layers are separated.



## 2. Rods & Cones layer =

dendritic processes of rod & cone cells = highly modified cilia

## 3. Outer limiting membrane =

Junctional complexes bet. rods & cones & Müller cell processes.

## 4. Out. Nuclear Layer :

Contains nuclei of rod & cone cells [1<sup>st</sup> Order Neurons]

## 5. Out. Reticular [plexiform] L :

Contains synapses bet. axons of rod & cone cells & dendrites of bipolar n. cells & horizontal cells.

## 6. Inner Nuclear L. :

Contains cell bodies & nuclei of 4 types of cells :

- (a) Bipolar n. cells [2<sup>nd</sup> Order N.] : they synapse & axons of rod & cone cells
- (b) Horizontal cells : } Their processes extend horizontally in the plexiform layers to integrate impulses from photoreceptors over a wide area of the retina.
- (c) Amacrine cells : }
- (d) Müller cells = Neuroglial supporting cells. Their cell bodies are present in inner nuclear L. Their long processes extend to the out. limiting memb. Also, microglia are scattered throughout the retina.

## 7. Inn. Reticular L. :

Where axons of bipolar cells synapse & dendrites of ganglion cells. Both synapse & processes of amacrine cells.

## 8. Ganglion Cell Layer :

Contain few large nerve cells [3<sup>rd</sup> Order N.]

## 9. Optic nerve fibres L =

= unmyelinated axons of ganglion cells & no neurolemma (cannot regenerate)  
The axons come out at right angle  $\rightarrow$  optic nerve.

## 10. Inn. limiting memb.

formed by tight junctions bet. the ends of processes of Müller cells.



## Rod & Cone Cells

The 1<sup>st</sup> order N. in the visual pathway. Formed of :

- Cell body (contain nucleus) • dendritic process (out. & inner segment)
- central process (axon).

|                | Rod Cell                                                                                                                                               | Cone Cell                                                                                    |
|----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|
| N <sup>o</sup> | 70 - 120 million                                                                                                                                       | about 7 million                                                                              |
| Out. Segment   | cylindrical (rod)-shaped<br>- contains flattened discs w contain the visual pigment rhodopsin<br>- discs are phagocytosed by pigment cells             | cone shaped.<br>- discs are infrequently shed off & phagocytosed by pigment cells            |
| Inn. Segment   | - connected to the outer segment by constriction (contain cilium)<br>- Site of ptn. synthesis (rich in mit., rER & G.A).                               |                                                                                              |
| Outer fibre    | - connects inner segment to the cell body.                                                                                                             | absent (only slight constriction)                                                            |
| Cell Body      | - contains the nucleus & sends an inner fibre (axon) w end by <u>spherule</u> } <u>pedicle</u><br>both synapse & dendrites of the bipolar nerve cells. |                                                                                              |
| Functions      | - Vision in dim light.<br>(by night) black & white                                                                                                     | - Bright light, colored vision & high visual acuity [the only receptors in fovea centralis]. |
| Clinical Notes | - Defecuity of vit. A →<br>" " rhodopsin<br>→ night blindness                                                                                          | lack of iodopsin in the cones<br>→ Color blindness.                                          |
| Site           | - mainly peripheral                                                                                                                                    | - mainly central                                                                             |

Macula lutea (yellow spot) = yellow depressed spot opposite to centre of the lens has fovea centralis in its bottom.

### Fovea Centralis:

The area of best visual acuity as At this area:

1. except for photoreceptor, most of the layers are reduced or absent.
2. Have cones only.
3. Highly transparent (no bl. vs.)

### Macular degeneration:

Age related → blindness in the centre of the visual field.



## Accessory Structures of Eye

Formed of:

### ① The Eye lid

1. Thin skin: e' fine hairs but no fat.

The lid margin contains 2-3 rows of eye lashes.

e' → apocrine sweat gls. = gls. of Moll.

→ sebaceous gls. = gls. of Zeiss.

2. Orbicularis Oculi & Levator palpebrae = skeletal ms.  
(facial expression ms.) (opens the eye)

3. Tarsal plate = dense c.t. w contains Meibomian's glands = modified sebaceous gland. Its oily secretion covers the tear film & its evaporation.

4. Palpebral Conjunctiva.

[Infl. of gls. of Moll → chalazion while infl. of gls. of Zeiss → Stye.]

### ② Conjunctiva

- transparent mucous memb.: 2 parts: Bulbar conjunctiva that covers the sclera & is reflected → to line the eye lid → palpebral conj.
- formed of Stratified col. epith. e' goblet cells resting on b.m. + lamina propria. At the limbus, the epith. changes gradually into str. sq. epith. e' no goblet cells.
- Function: mucous formed by goblet cells, form part of the tear film → to protect the epith. of ant. part of the eye.

[Inflammation of conj. → redness & watering of eye, so called Pink eye]

### ③ Lacrimal Apparatus

• The lacrimal gland:

Comp. tubulo-alveolar serous gl. w secrete tears. The acini are lined by Col. cells and surrounded by myoepithelial cells.

• Lacrimal canaliculi:

w drain the tears. lined e' st. sq. epith. →

• Lacrimal sac:

dilated part. lined e' ps. st. col. cil epith. →

• Nasolacrimal duct:

drains tears to nose " " " " " "

[Stenosis of the canaliculi or obstruction of the nasolacrimal duct →

Obstruct<sup>n</sup> & infl. of the lacrimal sac.]



## I External Ear

1. **Ear Pinna** = Funnel shaped elastic cartilage, covered on both sides by skin

2. **Ext. auditory meatus**:

- It's outer  $\frac{1}{3}$  is the continuation of the auricle so, supported by elastic cartilage. It's inner  $\frac{2}{3}$  is a bony canal.
- lined e' skin e' hair follicles, sebaceous & Ceruminous glands [apocrine sweat glands] → cerumen = yellowish oily/waxy contains ptns., FAs., sloughed Keratinocytes. Funct<sup>2</sup>: protective & antimicrobial.

3. **Ear drum [tympanic memb.]**

= 2 ls of collagen fs (inner circ. & out. radial) + elastic fs + fibroblasts.

It's outer surface is covered e' stratified squamous epith. &

" inner " " " " simple cuboidal "

It's anterosuperior quadrant is flaccid & transparent (e' no collagen fibres & called **Shrapnel's membrane** [Pars Flaccida].

**Perforation of tympanic memb.** → transient or permanent defective hearing.

## II Middle Ear

Air filled cavity in the temporal bone. lined e' s. cub. epith.

It's **lat. wall** = ear drum.

It's **med. "** is in contact e' the inner ear via the round & oval windows.

The Oval window: closed by the foot of stapes. transmits vibrations of ear drum to perilymph in inner ear.

The round ": closed by elastic memb. (2<sup>ry</sup> tympanic memb.) & dissipates sound waves after stimulating the receptors

Posteriorly: continuous e' mastoid cavities of mastoid air cells.

Anteriorly: connected to nasopharynx by Eustachian (auditory) tube.

It contains:

1. **Bony Ossicles (3)**: Malleus, Incus & Stapes.

The handle of malleus is attached to the tympanic memb. while the foot of stapes fits into the oval window. They articulate by synovial joints & covered e' s. cub. epith.

2. **Muscles**: Tensor tympani inserted into the malleus & stapedius inserted into stapes.

They regulate conduct<sup>2</sup> of sound. loud sounds → reflex contract<sup>2</sup> to limit vibration of the ear drum & stapes & prevent damage of recepto



### 3. Chorda tympani.

Conductive Deafness: is due to diseases of ext. aud. canal, ear drum or ossicles.

#### The Eustachian tube: (auditory tube)

- 4 cm long. Connects middle ear to the nasopharynx.
- Opens during yawning or swallowing to equalize pressure on both sides of ear drum. - lined e' ps. st. col. cil. epith. Goblet cells are present only in  $\frac{1}{5}$  of it.
- At the pharyngeal side, a tubal tonsil is present.

Otitis media: infection spread from the nasopharynx to the middle ear via auditory tube.

### III - Inner Ear

#### a - Bony Labyrinth:

1. Cochlea.
2. Vestibule
3. Semicircular canals.

Filled e' perilymph (e' high  $\text{Na}^+$  & low  $\text{K}^+$ )  $\xrightarrow{\text{drain into}}$  subarchnoid space.

#### b - Membranous labyrinth:

inside the bony labyrinth includes:

1. Cochlear duct.
2. Utricle & saccule
3. membranous semicircular canals.

Filled e' endolymph (e' low  $\text{Na}^+$  & High  $\text{K}^+$ )  $\xrightarrow{\text{drain into}}$  Dural venous sinuses.

#### A. The Cochlea

- A bony tube w makes  $2\frac{1}{2}$  turns around a central bony axis called **modiolus** = spongy bone w contains: bl. vs, nerve fibres & spiral gang.
  - A bony projection = **spiral lamina** extends from the modiolus into the lumen of the cochlear tube.
  - The periosteum of the outer bony wall of cochlea is thickened  $\rightarrow$  Spiral ligament.
  - The basilar memb. extends from the spiral lamina to spiral lig. & carry Organ of Corti.
  - The vestibular memb. extends " " " " to wall of cochlea.
  - The bony cochlea appear as 5 cavities around the modiolus. each cavity is subdivided into:
    1. **Scala Vestibuli**: above the vestibular memb. contains perilymph.
    2. **Scala Media** = Cochlear duct, contains endolymph.
    3. **Scala tympani** = below basilar memb. contains perilymph.
- Both, scala vestibuli & scala tympani are lined e' s. sq. epith.



## The Cochlear duct:

- 3 -

- Triangular space filled w' endolymph & conned to the saccule
- It's floor = Basilar memb. = s. sq. epith. & b.m.
- It's roof = Vestibular " " " = 2 layers of s. sq. epith. joined by tight junctions to preserve high ionic gradient bet. perilymph in scala vestibuli & endolymph in the cochlear duct.
- It's lat. wall = Stria Vascularis = ps. st. col. epith (unusually vascular + vascular c.t. It forms the endolymph. The cells have basal infoldings →  $K^+$  pump into the cochlear duct in the form of endolymph.

## Organ of Corti

Neuroreceptor for hearing, on the basilar memb inside Cochlear duct. Formed of:

### (1) Hair [Sensory] Cells:

- a. Inner hair cells: 1 row supported by inner phalangeal cells.
- b. Outer " " : 3-4 rows " " outer " " " "

Both inner & outer cells are provided w' long microvilli (Stereocilia) that act as receptors. Their bases are provided w' nerve endings = dendrites of bipolar nerve cells of spiral ganglia. The apical stereocilia are embedded in a gelatinous memb. called Tectorial Membrane [= glycoprotein + collagen bundles]

### (2) Supporting Cells:

#### a. Inner & outer phalangeal Cells:

- They rest on the basilar memb. & directly support the hair cells.
- The out. phalangeal cells form 3-4 rows & each have cup shaped apex w' surround the basal  $\frac{1}{3}$  of the outer hair cells & extends one phalanx w' is joined to the hair cell by junctional complexes.
- The inner phalangeal cells form one row w' completely surround the inner hair cells.



## b. Inner & outer pillar cells :

-4-

The outer cells have upper expanded end w fits into the upper concave end of the inner cells & form boundaries of **Tunnel of Corti**. They contain **Keratin bundles** → cytoskeleton (support)

c. **Hensen's Cells**: tall col. cells adjacent to out. phalangeal cells.

d. **Cells of Claudius**: short " on the out. edge of organ of Corti.

e. **Border Cells**: support the inner side of organ of Corti.

**Neural deafness**: due to loss of hair cells of organ of Corti or degenerat<sup>n</sup> of the cochlear nerve. treated by cochlear implants.

## B. The Vestibule

- A bony cavity containing the utricle & saccule
- Both are formed of c.t. lined e' s. sq. epith. They are connected to the periosteum by c.t. strands.
- They have neuroepith. structures called **macula** (تشعشع)
- Macula of saccule is perpendicular to the macula of utricle.

## C. The Semicircular Canals

- 3 bony semicircular canals w contain 3 membranous canals surrounded e' perilymph & attached to the bony canals by c.t. strands.
- Each canal has a dilated end called **ampulla**. It contains neuroepith. structure called **Crista ampularis**. (تشعشع)

| Macula (utriculi & sacculi)                                                                                                                                            | Crista ampularis                                                                                      |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|
| <b>Hair Cells</b> = mechanoreceptors e' apical stereocilia (e' actin core) + 1 true cilium = Kinocilium (e' basal body). Type I (flask shaped) + type II (cylindrical) |                                                                                                       |
| <b>Supporting cells</b> Col. cells e' basal oval nuclei. present bet. the hair cells. Have apical microvilli                                                           |                                                                                                       |
| <b>Covered e'</b> thick gelatinous glycoprotein memb. contains <b>CaCO<sub>3</sub> crystals</b> called <b>Otolithic memb.</b>                                          | Formed by the supporting cells has <b>no CaCO<sub>3</sub> crystals</b> called <b>Cupula</b> & thicker |
| <b>Function</b> register linear acceleration & deceleration of the head.                                                                                               | register rotational acceleration.                                                                     |

**Defective vestibular apparatus** → Vertigo  
**Overstimulation of macula** → motion sickness.



## General Characters of CNS.

1. Protected by bone
2. covered e' meninges.
3. soft (jelly like) (no c.t)
4. Formed of grey matter & white matter (presence of myelin)

### Parts of CNS:

#### I. Brain

1. Cerebrum.
2. Cerebellum.
3. Diencephalon (thalamus, subthalamus, epithalamus)  
hypo "
- 4 Brain stem (midbrain, pons & medulla).

#### II Sp. cord

(31 segment)

8 cervical

12 thoracic

5 lumbar

5 sacral

1 coccygeal.

| <u>Grey matter</u>                                                                              | <u>White matter</u>                                                                             |
|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|
| Formed of • nerve cells + unmyelinated n. fibres + neuroglial cells.                            | myelinated nerve fibres + neuroglial cells.                                                     |
| Parts • 2 post. horns + 2 ant. horns + Commissure + [2 lat. horns in thoracic & upper 2 lumbar] | - post., lat. & ant. columns.                                                                   |
| * <u>The post. horns</u> : contain sensory nuclei.                                              | * <u>Post. Column</u> :<br>[bet. dorsal septum & post. horn]<br>Contains ascending tracts only. |
| * <u>The lat. horns</u> : " sympathetic "                                                       | * <u>Lat. column</u> : bet post & ant. horn                                                     |
| * <u>The ant. "</u> " motor nuclei                                                              | * <u>Vent. column</u> :<br>[bet. ant. column & vent. fissure]                                   |
| * <u>The commissure</u> : " commissural "                                                       | - the lat & vent. columns contain ascending & descending tracts.                                |

|                              | <u>Cervical</u>                                                               | <u>Thoracic</u>                                            | <u>Lumbar</u>                                                                                          |
|------------------------------|-------------------------------------------------------------------------------|------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|
| - Outline                    | Oval                                                                          | rounded                                                    | rounded.                                                                                               |
| - Site of c.c.               | Ventral                                                                       | slightly ventral                                           | central                                                                                                |
| - Grey matter                | <u>4 horns</u> :<br>- 2 thin diverging post. horns.<br>- 2. thick ant. horns. | <u>6 horns</u> :<br>- 4 thin horns<br>- 2 small lat. horns | <u>4 horns</u> :<br>- 2 thick/ parallel post. horns.<br>- 2 thick ant. horns<br>- lat. horns in L1 & 2 |
| - White : grey matter ratio. | Largest                                                                       | - large                                                    | - smallest.                                                                                            |
| - Gracil & cuneate           | present                                                                       | - G. & cuneate in T <sub>1-6</sub><br>small                | - Gracil. No cuneate<br>- large                                                                        |



## Pathway of proprioception & fine touch [From body]

Proprioception = sense of position, vibration & movement.

Fine touch = Tactile localisation, tactile discrimination & stereognosis.

Receptors for Proprioception

- Pacinian Corpuscle : in c.t. capsule of joint
- muscle spindle : in muscles.
- Tendon " " tendons

Receptors for fine touch:

1. Merkle's disc
2. Meissner's corpuscle
3. Ruffini organ.

### First Order Neuron:

- Large cells of spinal ganglia:-  
Have peripheral branch = thick myelinated nerve fibres w̄ receive sensation from receptor. Their central branches enter the sp. cord through the medial division of post. root. The fs. divide into long ascending & short descending branches.
- long ascending fs in sacral, lumbar & lower thoracic segments ascend as gracile tract
- long ascending fs. in upper thoracic & cervical " " Cuneate tract
- Gracile & Cuneate tracts ascend to end on cells of:

### Second Order Neuron:

- Cells of Gracile & cuneate nuclei of closed medulla (upper  $\frac{1}{2}$ ) (same side).
- Axons of these cells form int. arcuate fibres w̄ cross to the opposite side forming sensory decussation & form the medial lemniscus. that ascend to end on c-

### Third Order Neuron:

Cells of Posterolateral Ventral Nucleus of Thalamus [PLVNT]  
Axons of these cells ascend in the sensory radiation to end in the sensory area in the post central gyrus of cerebral Cortex [area 3, 1 & 2].

Lesion of Gracile & Cuneate tracts of the sp. cord →  
ipsilateral loss of proprioception & fine touch in the limb below the lesion.



## Gracile tract

- long ascending sensory tract
- In post. column of white matter of spinal cord (**all levels**)
- large cells of spinal ganglia of **sacral, lumbar & lower thoracic** segments
- Their peripheral branches (thick myelinated) " central branches enter the sp. cord through the **med. division** of post roots. then ascend to terminate in:
- **Gracile Nucleus** in closed medulla (same side)

Carry proprioception & fine touch from the lower  $\frac{1}{2}$  of the body (same side)

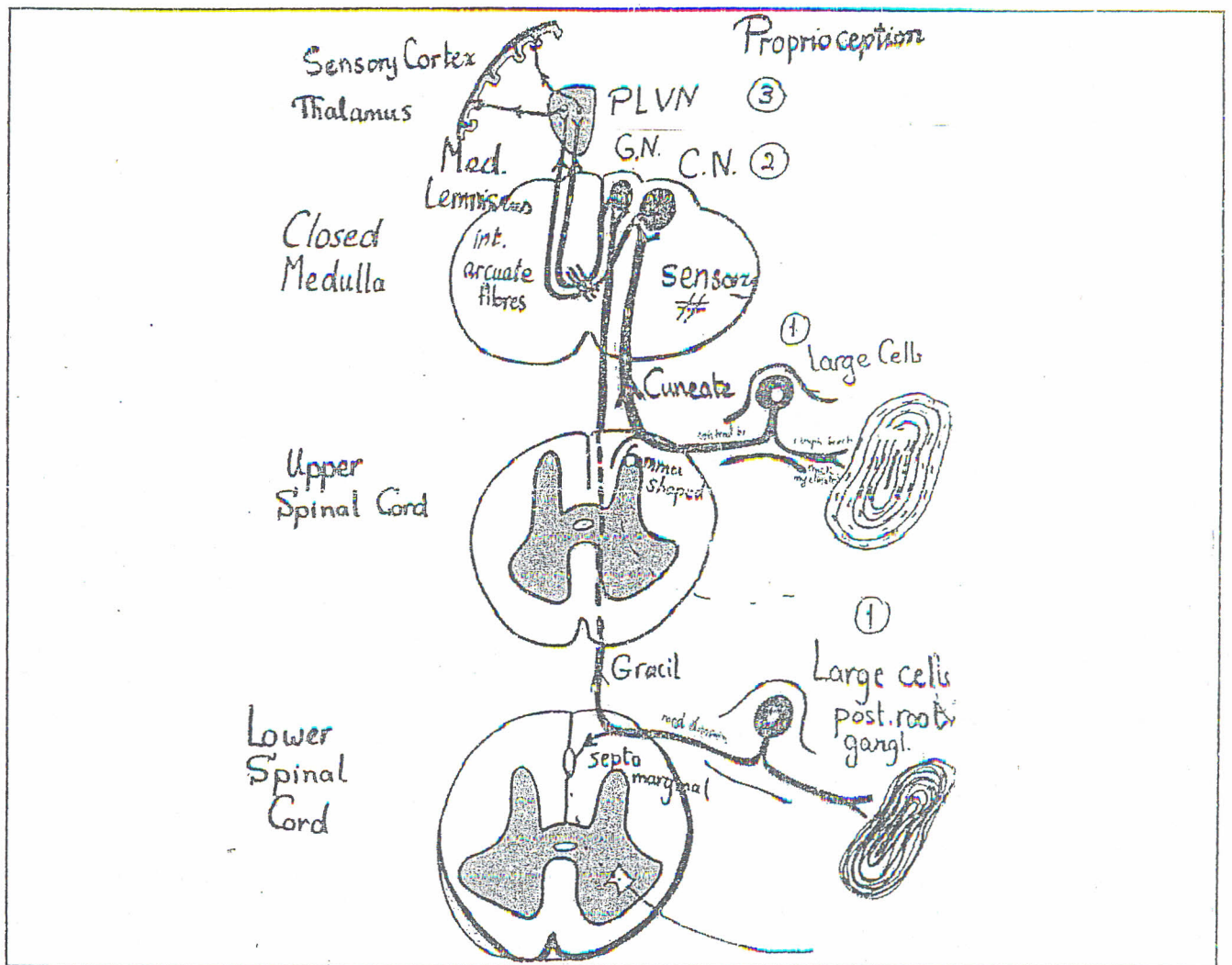
## Medial Lemniscus:

- ascending sensory bundle in the brain stem
- Cells of gracile & Cuneate nuclei of closed medulla of the opposite side
- axons of these cells form internal arcuate fibres w cross to the opposite side forming sensory decussation then ascend as med. lemniscus to
- **thalamus**: Cells of PLV N of thalamus.
- Carry proprioception & fine touch from the opposite side of the whole body.

## Cuneate tract

- long ascending sensory tract
- In post. column of white matter of sp. cord (In **cervical & upper thoracic** levels only)
- large cells of spinal ganglia of **upper thoracic & cervical** segments.
- Have peripheral branches = thick myelinated & central branches w enter the sp. cord through the **med. divisions** of post. roots. then ascend to terminate in:
- **Cuneate Nucleus** in closed medulla. (same side).
- Carry proprioception & fine touch from the upper  $\frac{1}{2}$  of the body (same side)





### Tabes Dorsalis:

Syphilis causes destruction of n.fs of post root at point of entrance to sp. cord. esp. (lower  $\frac{1}{2}$ ). causing:

1. Stabbing pain, parathesia & numbness in lower limbs.
2. Hypotonia (loss of proprioception from ms & joints).
3. Sensory ataxia in lower limbs → unsteady gait compensated by vision. On closure of eyes or in the dark, patient may fall.
4. loss of Knee & ankle tendon reflexes.



# Pathway of Pain & Temperature [from body]

-4-

Receptor: free nerve endings.

1st Order Neuron:

= **Small** cells of the spinal ganglia.

Their peripheral branch = thin myelinated nerve fibres w receive sensation from receptor. Their central branches enter the sp. cord through the **lateral** division of the post. root & form **Lissauer's tract** w ascend or descend 1 or 2 segments to end on cells of:

2nd Order Neuron:

= Cells of **Substantia Gelatinosa of Rolandi S.G.R.**

Axons of these cells cross to the opposite side in front of the central canal & ascend as the **Lat. spino-thalamic tract** in the lat. column of the white matter & brain stem. In the pons, it joins the vent. spino thalamic tract to form the **Spinal lemniscus** that ends in: →

3rd Order Neuron:

= Cells of **posterolateral Ventral Nucleus of Thalamus [PLVNT]**

Their axons ascend in the sensory radiation to reach the sensory area in the post central gyrus of cerebral cortex [area 3, 1 & 2]

# Pathway of Crude Touch [from body]

Receptors:

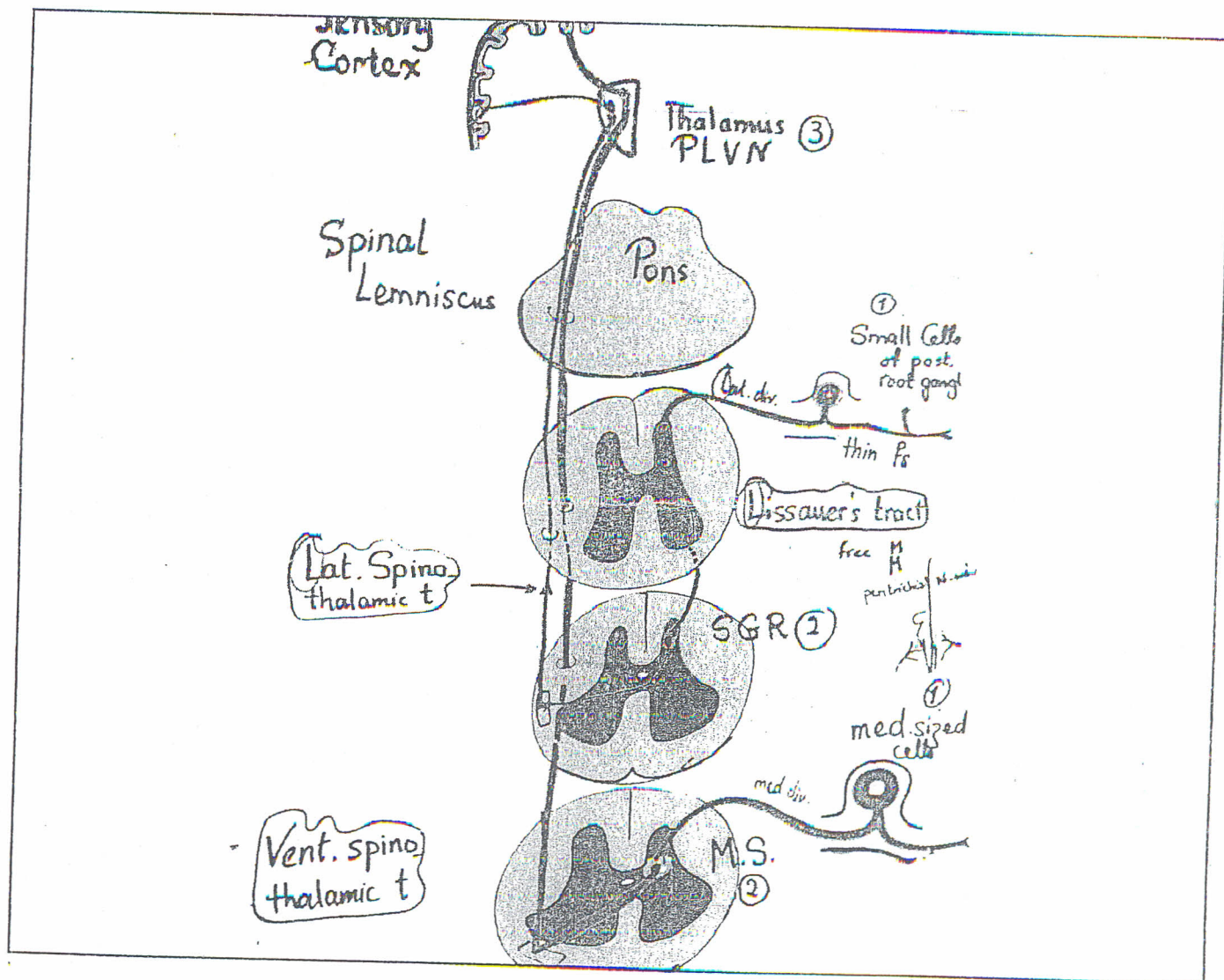
1. free nerve endings
2. peritrichial nerve endings.
3. Merkle's disc
4. Meissner's Corpuscles

1st Order Neuron:

= **Medium sized** cells of the spinal ganglia.

Their peripheral branch (**med. sized** myelinated n. fibres) receive sensation from the receptors. Their central branches enter the spinal cord through the **medial** division of the post. root to end on cells of:







= Cells of **Main Sensory N. [Nucleus Proprius]**

Their axons cross to the opposite side in front of the c.c. to form the **Ventral spinothalamic tract** in the vent. column of white matter of brain stem. In the pons, it joins the lat. sp. thalamic t to form **Spinal Lemniscus** w end on cells of:

### 3rd Order Neuron:

= Cells of **PLVNT**. Their axons ascend in sensory radiation to end in sensory area in the post central gyrus of cerebral cortex (area 3, 1 & 2)

| <b>Lat. Spinothalamic tract</b>                                                                                                                                                       | <b>Vent. sp. thalamic t.</b>                                                                                                                                  |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>def</b> - long ascending sensory tract.                                                                                                                                            | - long ascending sensory tract.                                                                                                                               |
| <b>site</b> - In <b>lat. column</b> of white matter of sp. cord (all levels)                                                                                                          | - In <b>vent. column</b> of white matter of sp. cord (all levels)                                                                                             |
| <b>Origin:</b> Cells of <b>SGR</b> of opposite side                                                                                                                                   | - Cells of <b>MSN</b> of opposite side                                                                                                                        |
| <b>Course:</b> axons of the cells <u>cross</u> to the opposite side & ascend <u>singly</u> lat. until the pons where it joins the v. sp. thalamic tract to form the spinal lemniscus. | - axons of the cells <u>cross</u> to the opposite side & ascend <u>singly</u> until the pons where it joins the lat. sp. th. tract to form the sp. lemniscus. |
| <b>Terminat<sup>n</sup>:</b> Cells of <b>PLVNT</b> (opposite side)                                                                                                                    | - Cells of <b>PLVNT</b> (opposite side)                                                                                                                       |
| <b>Funct<sup>n</sup>:</b> Carry pain & temp. From " " of body.                                                                                                                        | - Carry Crude touch from " " of body.                                                                                                                         |
| <b>Lesion:</b> Contralat. loss of pain (pinprick) & temp. (hot & cold) below the lesion.                                                                                              | - Contralat. loss of Crude touch (piece of cotton) below the lesion.                                                                                          |

## Spinal Lemniscus

**def:** Ascending sensory bundle present in the brain stem. Formed by union of the lat. & vent. spinothalamic tracts. يشرحوا

**Origin:** the lat. sp. thalamic (cells of **SGR**) & vent. sp. thalamic (cells of **MS**) of opposite side

**Course:** axons of these cells cross to the opposite side as lat. & vent. sp. thalamic tracts. In the pons they join → sp. lemniscus

**Termination:** Cells of **PLVN** of thalamus.

**Function:** carry pain & temp. + crude touch from the opposite side of body.

**N.B** the fs. for pain are ant. while fs. for temp. are post. in position.



## Syringomyelia:

Congenital dilatation of C.C. of sp. cord in lower cervical & upper thoracic segments → press on lat. sp. thalamic t. → bilat. loss of pain & temp. in chest & upper limbs, while touch is preserved → dissociated sensory loss.

## Pathways from the Face & Head

### Pain & Temp. pathway

Receptors: free n. endings.

1st Order N: Cells in trigeminal ganglion

2nd Order N: Cells of spinal N of trigeminal nerve. axons cross & join the Trigeminal lemniscus

3rd Order N: Cells of PMVN of thalamus. Axons end in sensory area of cereb. cortex

### Crude Touch Pathway

Receptors: as in the body.

1st Order N: Cells in trigeminal ganglion.

2nd Order N: " " Main sensory N. Their axons cross & join the trigeminal lemniscus.

3rd Order N: Cells of PMVN of Thalamus. Axons end in sensory area of cereb. cortex

### Proprioception & fine touch Pathway

Receptors: Muscle spindle & tendon spindle in muscles of mastication + Pacinian corpuscles in deep dermis.

1st Order N: Mesencephalic Nucleus (inside CNS). Their axons descend to end on

2nd Order N: Cells of Main sensory N. Their axons cross to join the trigeminal lemniscus.

3rd Order N: Cells of PMVN of thalamus. Axons end in sensory area of cereb. cortex.

## Trigeminal Lemniscus

def: ascending sensory bundle in the brain stem.

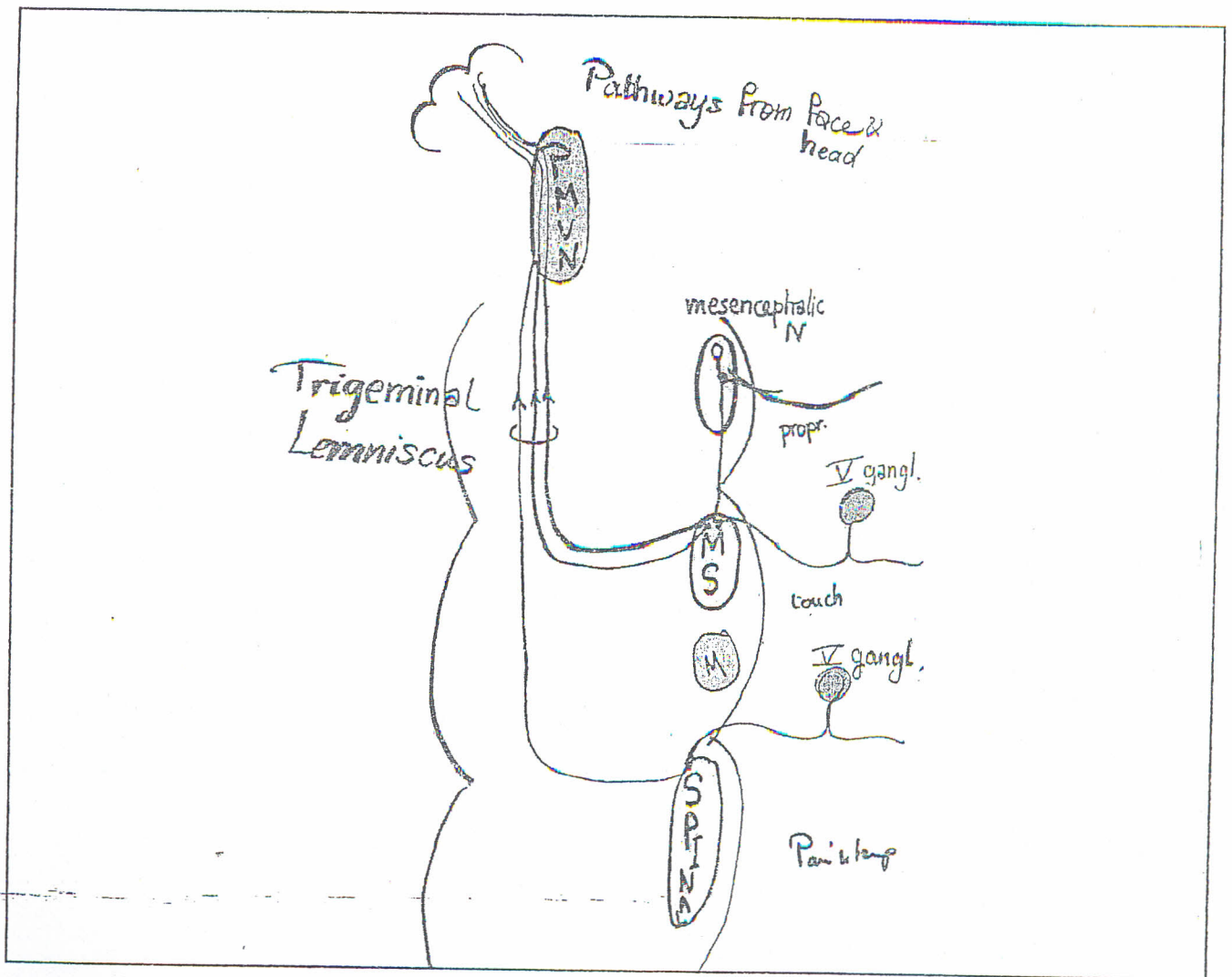
Origin: Spinal nucleus & main sensory nucleus of trigeminal nerve.

Course: Their axons cross to the opposite side & join to form the trigeminal lemniscus in pons & mid brain & end in:

termination: PMVN of thalamus.

Function: carry pain, temperature, crude touch & proprioception from face & head (scalp) [opposite side].







# Pathway of Sensory Impulses to Subcortical levels

## 1. Dorsal Spino Cerebellar t. (post)

**Origin:** Clark's N [C<sub>8</sub>-L<sub>2</sub>] on same side

It receives propriocept<sup>n</sup> from large cells in the spinal ganglia (so it is the 2<sup>nd</sup> order N in the pathway)

**Course** In Sp. cord in lat. column of white matter of upper lumbar thoracic & cervical segments + Closed medulla

**Termination** enter the cerebellum through the Inf. cerebellar peduncle

**Functions**- carry proprioception from trunk & lower limb to cerebellum  
Coordinate limb ms. & maintain posture

## 2. Vent. Spino-cerebellar t. (ant)

- Cells in Post. horn of grey matter in lumbosacral region [V-VII] on same & opposite sides.
- Receive proprioception from large cells in spinal ganglia. (2<sup>nd</sup> Order N.)
- In sp. cord in lat. column of the white matter at all levels + brain stem

- enter the cerebellum through the Sup. cerebellar peduncle

- Carry proprioception from lower limb to cerebellum.
- Coordinate " movement & maintain posture

## 3. Spino-Olivary t.

**Origin:** post. horn cells (laminae IV & V) of the opposite side. Receive propriocept<sup>n</sup> from large cells of spinal ganglia.

**Course:** ascends in the sp. cord. (all levels)

**Termination.** Inf. olivary N in medulla.  
It sends olivocerebellar fibres to cerebellum through ICP.

**Function:** carry proprioception to the cerebellum.

## 4. Spino-tectal t.

- P. HCs. (laminae IV & V) of the opposite side. Receive impulses from spinal ganglia.

- ascends in the sp. cord (all levels) + brain stem.

- Sup. colliculus of midbrain.

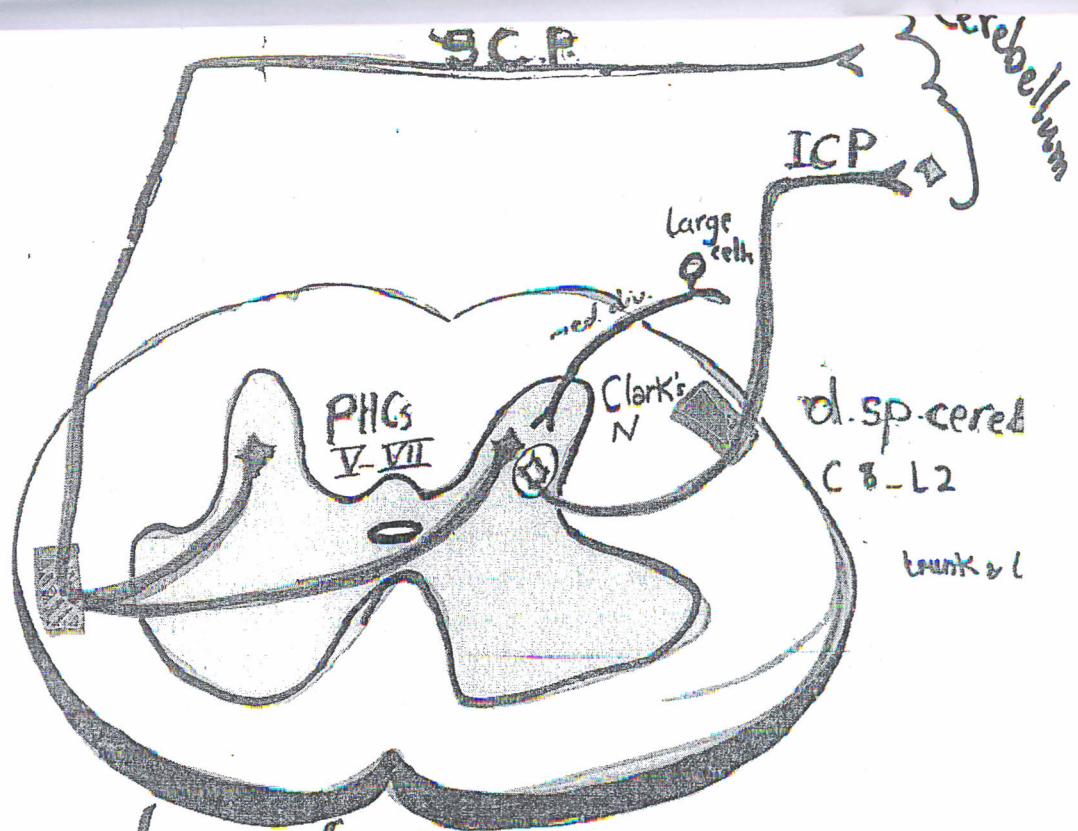
- carry sensory impulses to the tectum (drives spino-visual reflex movement of eye & head towards source of stimulation).

**N.B:** Unconscious proprioceptive pathway from the upper 1/2 of body [No Clark's N. above C<sub>8</sub>]

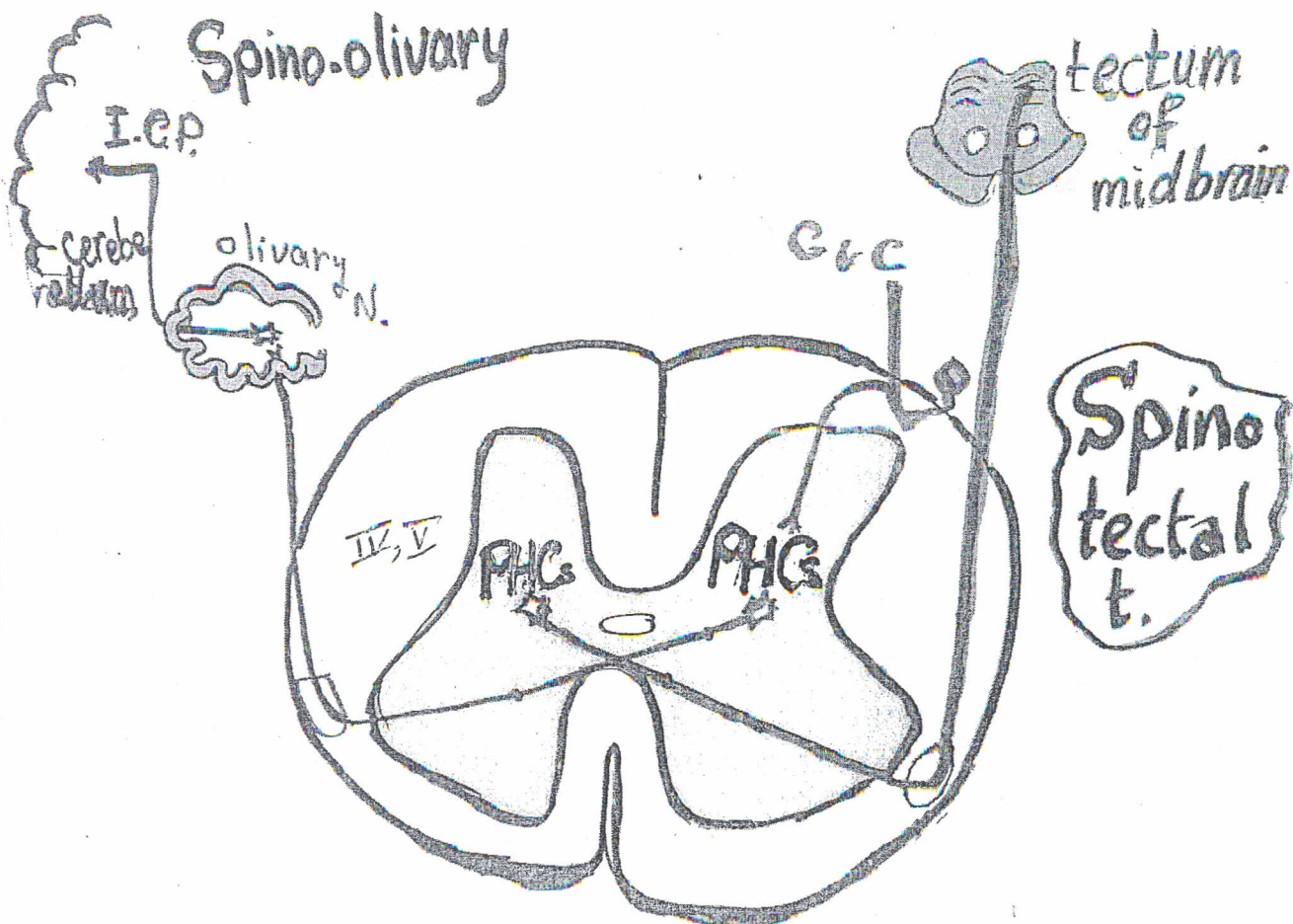
1<sup>st</sup> Order N: cells of sp. ganglia.

2<sup>nd</sup> " " : Accessory Cuneate N. (in medulla) ICP → cerebellum (same side).





Dorsal & Vent sp. cerebellar t





## SHORT TRACTS

-8-

def. tracts that start & end in the sp. cord.

### 1. Fasciculi proprii :

= axons of associative neurons bet. PHCs & AHCs

- Ascend or descend 1 or 2 segments outside the grey matter (like ring)
- enter the grey matter to end around cells of other segments.

F.: Coordinate function of different segments of sp. cord.

In the fetus, they are the 1<sup>st</sup> to be myelinated to coordinate its early movements.

### 2. Lissauer's tract :

def. short tract at the tips of post. horn of all segments.

Origin: small cells of the spinal ganglia. Their axons enter the sp. cord through the lat. division of post. root then ascend or descend 1 or 2 segments to end on: Cells of SGR [Substantia Gelatinosa of Rolandi.

Function: carry pain & temp. from same side of the body.

### 3. Septomarginal tract

Site post. column of white matter in thoracic, lumbar & sacral segments

= Short descending fibres from Gracile tract.

end on : AHCs

Function : Completes stretch reflex arc.

### 4. Comma shaped tract

Site: Post. column of white matter in Cervical & upper thoracic segments.

= Short descending fibres from Cuneate tract.

end on AHCs.

Function : Completes stretch reflex arc.



# Pyramidal tract

## 1. Cortico-spinal tracts:

- Fibres arise from cerebral cortex & terminate on AHCs of the sp. cord.
- Origin: Betz cells & other cells in motor area 4 (upper 2/3) of cerebr. cortex.
  - Course: axons descend in Corona radiata then in
    - Genu & ant. 2/3 of post limb of int. capsule →
    - Basis pedunculi of the midbrain (intermediate part) →
    - Basis pontis " " pons. Fibres are separated by t.v. pontine fibres.
    - pyramid in upper medulla. In the lower part of closed medulla, 85% of the fibres cross to the opposite side → motor decussation
    - In the sp. cord the crossed pyramidal tract is present in the lat. column of the white matter in all levels while the direct pyramidal is present in the ant. column of white matter in cervical & upper thoracic.
  - Termination: In AHCs of the opposite side. Some end on the same side. The direct Δ gradually crosses to the opposite side. few fibres end on the same side.
  - Function: Control voluntary movement. ↑↑ tone & reflexes in muscles (Facilitatory to fine & skilled movement)

## 2. Corticobulbar tracts:

Fibres arise from cerebral cortex & terminate on motor nuclei of cranial nerves in the brain stem:

### a. Medial Cortico-bulbar:

- Origin: motor area 8 in cerebral cortex.
- Course: The axons descend in corona radiata then in Genu of int. capsule
  - In the midbrain they are present in the basis pedunculi close to middle line
- Termination: motor nuclei of cranial nerves 3, 4 & 6 of both sides.

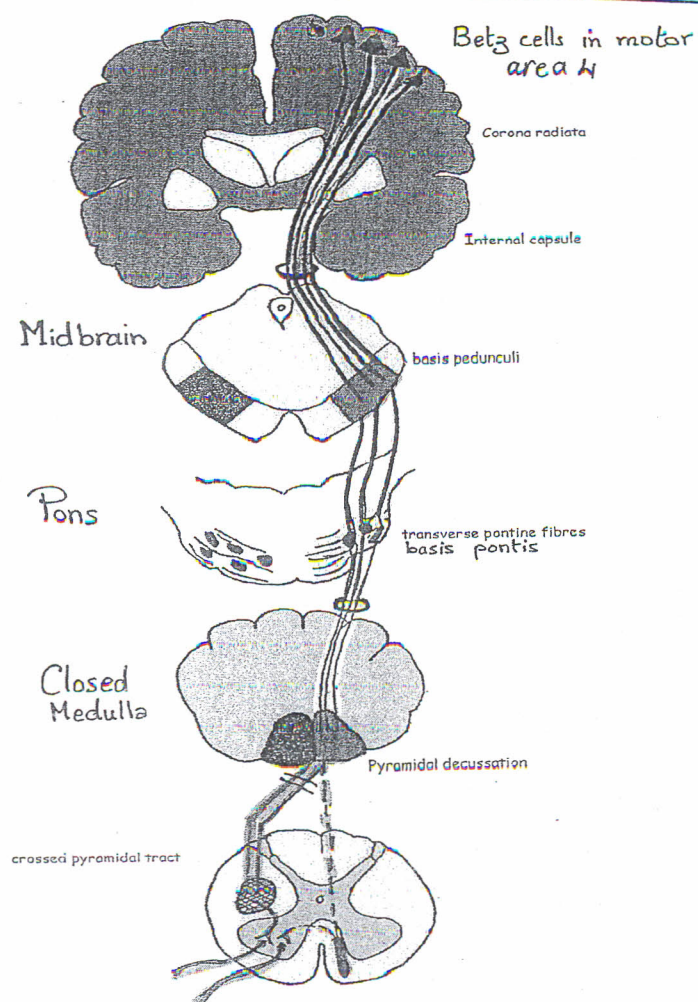
### b. Lat. Cortico-bulbar:

- Origin: motor area 4 (lower 1/3) in cerebral cortex.
- Course: Axons descend in the corona radiata then in the Genu of int. capsule
  - In the midbrain, they pass in the basis pedunculi lat. to corticospinal t.
- Termination: motor nuclei of cranial nerves 5, 7, 9, 10, 11 & 12 on both sides except:
  - the part of 12 that → protrudes the tongue.
  - " " " 7 → innervates the ms of the lower face.

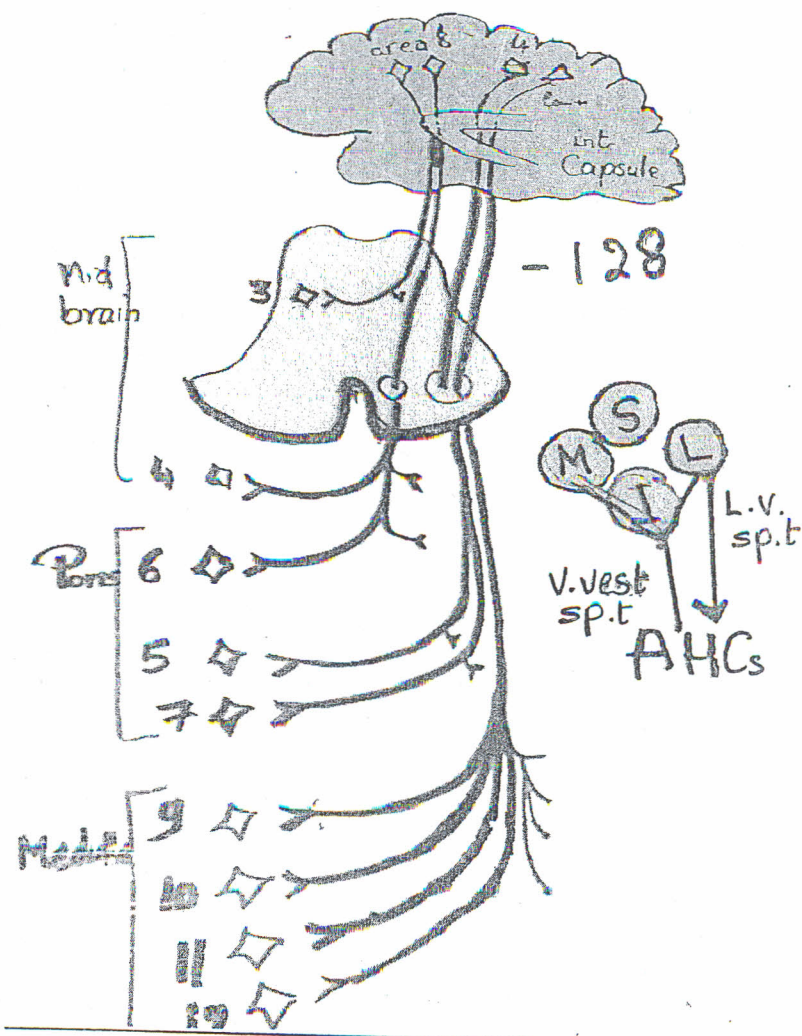
They receive contralateral innervation.



# Cortico-spinal t.



## Cortico-bulbar





- Extrapyramidal
- = Descending motor tracts w do not pass through the pyramids. 2 group
- (1) Tracts that arise from cerebral cortex & end in the brain stem.
  - (2) " " " " Brain stem & " " AHCs of spinal cord.

### Extrapyramidal tracts of the spinal cord

| Single tracts     | Paired tracts             |
|-------------------|---------------------------|
| • Rubro-spinal.   | • Lat. & vent tectospinal |
| • Olivo. " "      | • " " reticulo " "        |
| • Sulco-marginal. | • " " vestibulo sp.       |

| tract              | Origin                                | type                            | termination                 | Function     |
|--------------------|---------------------------------------|---------------------------------|-----------------------------|--------------|
| Sulcomarginal      | Continuation of the med. long. bundle |                                 | AHCs [All levels]           | Associative  |
| Rubro-spinal       | Red N. in (midbrain)                  | Crossed in (vent. tegmental #)  | AHCs, (cervical & thoracic) | Inhibitory   |
| Olivo-spinal       | Inf. Olivary N.                       | direct                          | AHCs (cervical)             | Facilitatory |
| lat. tecto-spinal  | Sup. colliculus                       | Crossed in (dorsal tegmental #) | AHCs (cervical)             | Inhibitory   |
| Vent " "           | (tectum of midbrain)                  |                                 | " (cervical, thoracic)      | " "          |
| lat. Vestibulo-sp. | lat. vestibular N.                    | direct                          | AHCs (all levels)           | Facilitatory |
| Vent " "           | lat., med. & inf. vestibular nuclei   | direct                          | AHCs (cervical)             | "            |
| lat. reticulo-sp.  | Reticular Formation in Brain stem     | - mainly crossed.               | AHCs (All levels)           | Inhibitory   |
| Vent " "           |                                       | - " direct.                     |                             | Facilitatory |

∴ 3 tracts rubrosp. } arise from midbrain & crossed  
 lat. & vent.  
 tectosp.

3 tracts - Olivo sp. } " " pons & medulla & direct.  
 lat. & vent.  
 vest. sp.

3 tracts Sulcomarginal + L. & V. reti. sp. from brain stem as a whole



## Med. longitudinal Bundle

-11-

**Def.:** associative bundle formed of ascending & descending myelinated nerve fibres.

**Site:** In the brain stem (near the middle line). Its continuation in the spinal cord is: ventral vestibulospinal tract + sulcomarginal tract.

**Connections & functions:**

### (1) Vestibular connections

#### a. Vestibulo-ocular:

- Connects vestibular nuclei & nuclei of 3, 4 & 6.

F. Coordinates eye movement & head movement.

#### b. Vestibulo-spinal:

- Connects vestibular nuclei [lat., med. & inf.] & AHCs [V. vest. sp. t.]

F. Coordinates head movement & neck & trunk movement.

### (2) Auditory Connections

- Connects Sup. olive + nucleus of trapezoid body + nucleus of lat. lemniscus & nuclei of 3, 4, 6, 7, 11 & 12.

F. Coordinates movement of eye, face, neck & tongue in relation to sound.

### (3) Cranial nerves Connections

- Connects nuclei of 3, 4 & 6 of both sides for conjugate eye movement.

- Connects " " 7, 11 & 12 so lips, larynx & tongue work together during speech.

### (4) Extrapyramidal Connections

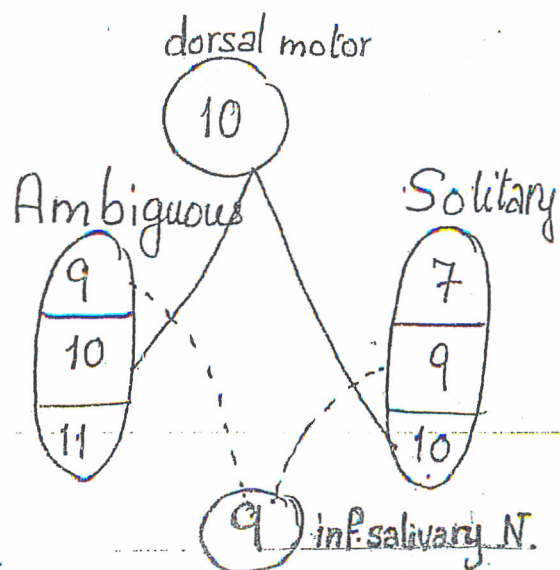
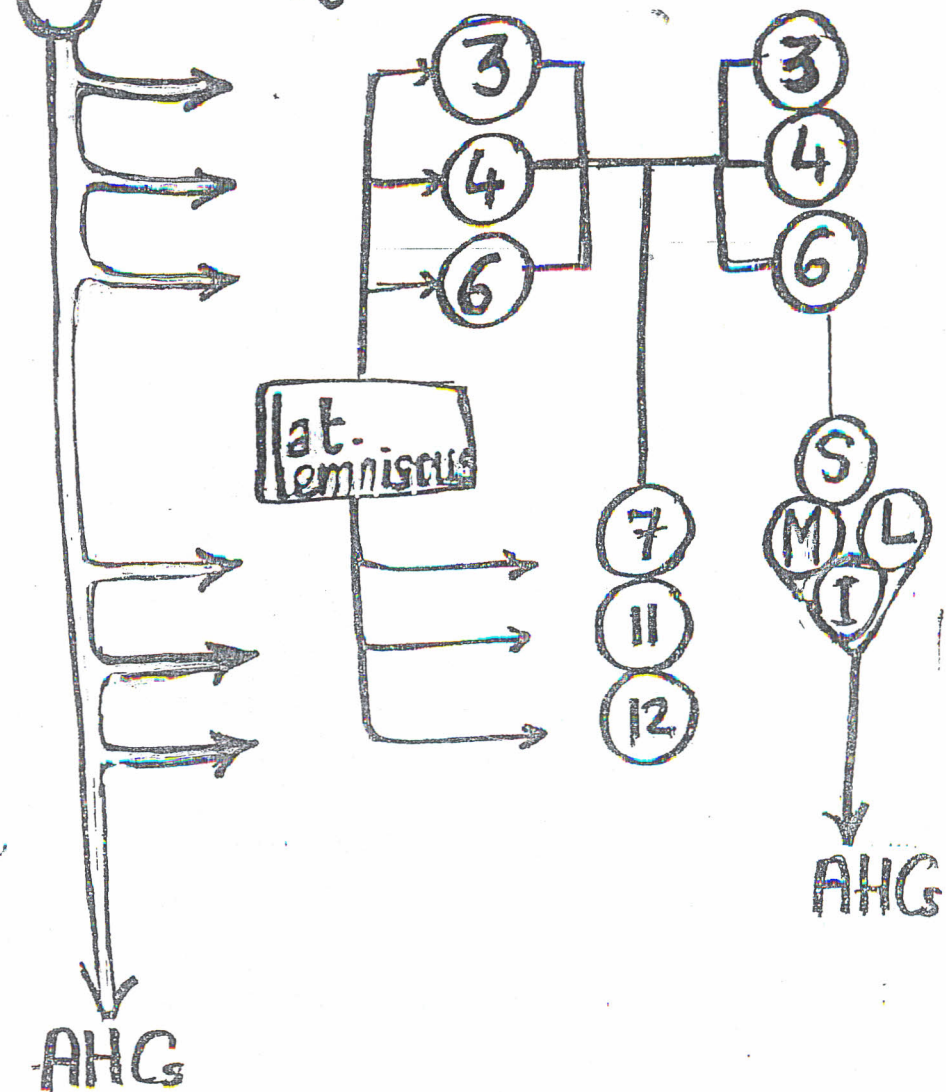
- Connects extrapyramidal nuclei → Interstitial nucleus of Cajal  
& → post. commissural nucleus  
& motor cranial nuclei & AHCs of sp. cord.

F. control movements of head, neck & trunk.



# MLB

Post. commissural N.  
N. of Cajal





## Visual Pathway

**Receptors**: rods & cones in retina.

**1st Order neurons**: Rod & cone cells in outer nuclear layer.

**2nd** " " : Bipolar nerve cells in inner " " " .

**3rd** " " : Ganglion cells in ganglion cell layer.

Axons of the ganglion cells form the optic nerve.

The nasal fibres cross to the opposite side forming optic chiasma.

The optic tract: contains temporal fibres of the same side & nasal fibres from the opposite side. Some fibres relay in the **Sup. colliculus** [visual reflexes]. Most of fibres relay in the **lat. geniculate body**. Their axons ascend in the **Optic radiation** to the visual area in **cereb. cortex** (area 17).

## Deep Origin of cranial Nerves in Medulla

**Hypoglossal Nerve (12)**: motor nucleus in floor of 4th ventricle.

**Accessory Nerve (11)**:  
 → lower part of nucleus ambiguus.  
 → AHCs of upper 5 or 6 cervical segments.

**Vagus Nerve (10)**:  
 → middle part of nucleus ambiguus.  
 → lower part of solitary nucleus.  
 → Dorsal motor nucleus.

**Glossopharyngeal Nerve (9)**:  
 → upper part of nucleus ambiguus.  
 → middle " " solitary nucleus.  
 → inf. salivary nucleus.

## Connection bet. Gracile & Cuneate nuclei & Cerebellum:

**Ext. arcuate fibres:**

**Post. ext. arcuate fibres**: enter ICP directly to cerebellum.

**Ant. " " "**: cross to the opposite side, enter the arcuate nucleus then ICP → cerebellum.



## Auditory Pathway

**Receptors:** Inner & Outer hair cells in Organ of Corti in cochlea.

### 1<sup>st</sup> Order Neurons:

= Bipolar nerve cells in spiral ganglia. Their axons form the cochlear nerve which enters the lower level of pons to end in:

### 2<sup>nd</sup> Order Neurons:

= Cells of dorsal & vent. cochlear nuclei: Their axons form the trapezoid body then cross to the opposite side & ascend as the lat. lemniscus. Some axons ascend in the lat. lemniscus of the same side.

Axons of the vent. cochlear nucleus relay in: sup. olive or nuclei of trapezoid body or lat. lemniscus.

Fibres of the lat. lemniscus relay in 2 sites 

inf. colliculus  
 Med. Geniculate body

### Final Order Neurons:

= Cells of the Med. geniculate body. Their axons pass in the auditory radiation to the auditory area in the temporal gyrus area 41 in Cerebral Cortex.

(N.B.) each lat. lemniscus carry hearing from both ears.  
 " MGB & each auditory area receives hearing from both ears.

### Lat. Lemniscus:

Origin: dorsal & vent. cochlear nuclei in inf. pons.

Course: Axons cross to opposite side → trapezoid body then lat. lemniscus

Terminate in: inf. colliculus & MGB.

Funct<sup>n</sup>: carry hearing from both ears but mainly from opposite side

∴ Brain lemnisci = 4

1. Med. lemniscus.      2. Spinal lemniscus.
3. lat.                      "                      4. Trigeminal                      "



## Vestibular Pathway

-14-

The vestibular nerve maintains equilibrium by coordinating reflexes of eye, neck & body according to position & movement of Head.

### Receptors : (5)

• Macula of utricle • macula of saccule • Crista ampularis (3)

• 1st Order neurons = bipolar n. cells in vestibular ganglia.

Their axons end in 5 places : Sup., inf, lat. & med. vestibular nuclei (2nd Order N) + direct fibres to the cerebellum = direct vest. cerebellar

Vestibular nuclei Connections : give 5 tracts :

### 1- Vestibulo ocular Connections :

Fibres from vest. nuclei pass in the M.L.B. to be connected to nuclei of III, IV & VI (eye movement) & body

F. Correlates eye movement & head movement. (make eye fixed on stationary point during head & body movement)

### 2- Vestibulo spinal Connections :

lat. vestibulo sp. t. : connects lat. vest. N. & AHCs.

Vent " " " " lat. med & inf. vest. nuclei & AHCs.

F. ↑↑ the tone of extensors of Leg. to support the body against gravity.

### 3- Vestibulo-bulbar Connections :

Fibres from the lat. vest. nucleus pass through MLB to reach the accessory N.

F. : ↑↑ the tone of extensors of the neck to support the head against gravity

### 4- Vestibulo-reticular Connection :

Fibres from the vest. nuclei pass through the MLB to reach the reticular formation of mid brain. F. stimulates Vomiting centre.

### 5- Vestibulo-cerebellar Connections :

Fibres from the sup. vest. N pass to the cerebellum [indirect vest. cerebellar]

Function : direct & indirect fs relay in the flocculonodular lobe → dentate Nucleus → thalamus → cerebral cortex [area 4, 6 & 8].

∴ Cerebellum Can influence the activity of the pyramidal tract.



## Deep Origin of cranial nerves in Pons

### Vestibulo-cochlear Nerve [VIII]

- Vestibular part: origin: bipolar n. cells in the vestib. ganglion & end in 4 vestibular nuclei (sup, inf., lat. & med) in pontomedullary junction.
- Cochlear part: origin: bipolar n. cells in the spiral gangl. & end in dorsal & vent. cochlear nuclei in inf. pons.

Facial Nerve VII: has 3 nuclei → motor N (in inf. pons)  
→ upper part of solitary N (sensory)  
→ sup. salivary N (parasymp) in R.F.

Abducent Nerve VI Abducent motor nucleus in inf. pons.

Trigeminal Nerve V: 4 nuclei

- mesencephalic Nucleus: in sup. pons + midbrain. Receives proprioception from face
- Motor: in middle pons: motor to ms. of mastication.
- Main sensory " " : receives crude touch from the face.
- Spinal Nucleus: in inf. pons & medulla: receives pain & temp. from the face.

### N.B. definitions:

- nucleus = Group of n. cells in CNS.
- tract = group of n. fibres " " have same origin, terminat<sup>n</sup> & funct
- lemniscus:

A bundle of sensory fibres in the brain stem. It terminates on specific nuclei in the diencephalon.

## The meninges

Pia matter: (tender mother)

- A single layer of modified fibroblast that overlap each other. Highly vascular
- Covers the surface of brain & sp. cord.

Arachnoid matter: (network of threads made by spider)

- 2 types of cells → border cells: joined by tight junctions & form the roof.  
→ trabecular cells: hold up the roof like pillars.
- Separated from pia matter by subarachnoid space w contains → CSF. & bl. vs.
- Together e' pia matter → a compound memb. called pia-arachnoid or leptomeninges.

Dura matter: (tough mother)

- 2 fibrous layers → Outer thick separated at sites of venous sinuses.  
→ inner thin



# Red Nucleus

def. : Oval mass of Grey matter in the midbrain at level of sup. Colliculus  
 1 Red in fresh section as it is highly vascular & rich in iron pigment  
 It is an extrapyramidal nucleus.

Receives afferent fs from:

1. Cerebral Cortex.
2. Globus Pallidus
3. Subthalamus
4. Cerebellum [opposite side]

Gives efferent fibres to:

1. Thalamus.
2. Rubro-reticular to R.F. (opposite side)
3. Rubro-bulbar to cranial nuclei ( " " )
4. Rubro-spinal " AHCs ( " " )
5. Rubro-olivary " inf. olivary N. ( " " )

|                          | Inferior Colliculus                                        | Sup. Colliculus.                                          |
|--------------------------|------------------------------------------------------------|-----------------------------------------------------------|
| Aqueduct                 | surrounded by quadrilateral shaped grey matter             | surrounded by pear-shaped grey matter.                    |
| Nuclei of Cranial nerves | Mesencephalic n. of trigeminal nerve + Trochlear Nucleus   | + Oculomotor Nucleus                                      |
| Tectum                   | Inf. colliculus = one mass = centre for auditory reflexes. | Sup. colliculus = 5 laminae = centre for visual reflexes. |
| Extra-pyramidal nuclei   | Substantia Nigra                                           | Substantia Nigra + Red N.                                 |
| Lemnisci                 | 4                                                          | 3                                                         |
| Decussation              | decussation of Sup.C.P.                                    | Dorsal & Vent. tegmental decussations.                    |

## Deep Origin of Cranial nerves in the Midbrain:

- Trochlear Nerve IV : trochlear Nucleus in inf. level of midbrain.

- Oculomotor N. III : origin : Oculomotor nucleus in sup. " "

formed of : 2 Edinger Westphal nuclei  
 1 central group &  
 2 lateral groups.



# Cerebellum

Formed of 2 cerebellar hemispheres conned by vermis  
Has many folds (folia), each formed of cortex [Grey matter] & medulla [white matter].

## Cerebellar Cortex = Grey matter

1. Molecular Layer: the outermost L. Contains:

- dendrites of Purkinje cells.
- parallel axons of granular cells that synapse e' dendrites of Purkinje cells. each Purkinje cell receives excitatory impulses from 100,000-200,000 parallel fibres.
- Climbing fibres, coming from the inf. olivary nucleus, carrying excitatory impulses & synapse e' dendrites of Purkinje cells.

- Inhibitory interneurons:  $\left\{ \begin{array}{l} \rightarrow \text{Stellate cells} \\ \rightarrow \text{Basket " } \end{array} \right\}$  both synapse e' dendrites of Purkinje cells.

2. Purkinje Cell Layer: the middle layer: Contains Purkinje cells = One row of large multipolar [pyriform] nerve cells w are the 1<sup>st</sup> neurons of cerebellar cortex. Their dendrites extend to the molecular layer & have many spiny branches.

3. Granular Layer: the innermost layer. Contains:

1. Granular cells: small closely packed stellate nerve cells e' short dendrites w synapse e' excitatory mossy fibres coming from pontine nuclei. They send their T-shaped axons = parallel fibres to the molecular layer to synapse e' dendrites of Purkinje cells.

### 2. Golgi Cells:

large cells e' branching dendrites. Their axons synapse e' granular cells & send inhibitory impulse

3. Axons of Purkinje cells, Mossy fibres, climbing fibres.

## Cerebellar Medulla = White matter

Contains only nerve fibres  $\left\{ \begin{array}{l} \rightarrow \text{afferent} = \text{climbing \& mossy fibres.} \\ \rightarrow \text{efferent} = \text{axon of Purkinje cells.} \end{array} \right.$

Cerebellar nuclei in the white matter: 4 nuclei

1. Fastigial.
2. Emboliform
3. Globose
4. Dentate



## Cerebellar Connections

### • Sup. Cerebellar peduncle : SCP

#### Afferent:

1. Vent. sp. cerebellar tract.
2. Tecto. cerebellar "

#### efferent:

1. Cerebello-rubro sp. t.
2. Cerebello-thalamocortical.

### • Middle Cerebellar peduncle : MCP

#### Afferent

1. Cerebro ponto cerebellar.
2. Cerebello " " (from the other side)

#### efferent

1. Cerebello ponto cerebellar. (to the other side)

### • Inf. Cerebellar peduncle : ICP

#### Afferent:

1. Dorsal sp. cerebellar tract.
2. Ext. arcuate fs.
3. Olivo cerebellar t.
4. Vestibulo " "
5. Reticulo " "

#### efferent

1. Cerebello-olivary t.
2. " vestibular t.
3. " reticular t.

## Cerebrum

The cerebral cortex = 6 layers :

1. Molecular layer = parallel fs from next layers + Horizontal cells of Cajal.
2. Outer granular L = small pyramidal cells + stellate nerve cells.
3. Out. pyramidal L = med. sized <sup>(8 μm)</sup> pyramidal cells [40-50 μm].
4. Inner granular L = stellate nerve cells.
5. Inn. pyramidal L = large pyramidal cells [100 μm] = Betz cells.
6. polymorphic cell L. = nerve cells of diff. types & shapes.



## Brain Barriers

### 1] Blood brain barrier :

def : the barrier bet. blood & nerve cells of the brain : formed of :

- tight junctions bet. non-fenestrated endothelial cells of the capillaries
- Thick continuous basement memb. of the capillaries.
- Vascular end feet of astrocytes implanted on " .

Function : 1- prevent harmful substances from reaching nerve cells.  
2- allows passage of nutrition & precursors of neurotransmitters by facilitated diffusion & active transport.

### 2] Blood CSF barrier :

def. : the barrier w separates blood from CSF. formed of :

- endothelium of choroid capillaries.
- Basement memb of " "
- " " of ependymal cells
- Tight junctions bet. " "

Function : 1- Protection 2. Maintenance & constancy of CSF.  
3. Selection of substances to pass from bl. to CSF.

### 3] Arachnoid Barrier :

- Def : the barrier bet. extracerebral capillaries & subarachnoid space.
- formed of : arachnoid cells joined by tight junctions & desmosomes.
- Functions : prevent substances leaving extracerebral capillaries from reaching subarachnoid space, nerve cells of brain & brain ventricles.

In fetus & newborn : B.B.B. is not fully developed so, toxic subs. e.g. bilirubin can enter the CNS → yellowing of the brain.

- Direct trauma, inflammation or toxin → breakdown the BBB allowing large molecules to enter the CNS.
- On administration of penicillin, only small amount can enter the CN. (toxic in high conc<sup>n</sup>.)
- In meningitis, the meninges become more permeable at the site of inflammation allowing sufficient antibiotic to reach the infection
- In brain tumors, bl. vs frequently have no BBB.
- In the hypothalamus, the bl. caps are fenestrated & no BBB → ptns. & small molecules may pass to CNS allowing modification of metabolic activity of this area of the brain → protecting the nervous tissue as a whole.



**Upper Motor Neuron** = n. cells in cereb. cortex or subcortical level  
& end on AHCs (or) motor nuclei of cranial nerves

**Lower Motor Neuron** = AHCs or motor nuclei of cranial nerves  
give axons that end on muscles.

## General rules for sensory Pathways

**1<sup>st</sup> Order Neuron** = Cells of spinal ganglia (same side).

**3<sup>rd</sup>** " " = " " PLVN of thalamus (opposite side).

**2<sup>nd</sup>** " " For proprioception & fine touch in medulla (same side)  
" " " " pain & temp + crude (simple) in sp. cord (" ")

Axons of 2<sup>nd</sup> Order neuron cross in:

- sp. cord (pain, temp. & crude touch).
- medulla (proprioception & fine touch).



# Thick Skin

(1)

Present in palms & soles. Formed of:

## I. Epidermis

= Keratinized str. sq. epith. Formed of Keratinocytes & Non-Keratinocytes.

### [A] Keratinocytes

= 85% of cells of epidermis, form Keratin. 5 layers:

#### 1. Basal Cell layer = Stratum basale = germinal L.

L.M. 1 layer of Columnar cells, resting on a clear & wavy basement memb.

- Have basal oval nuclei w show mitotic figures for renewal w takes place every 2-4 weeks mostly at night. & basophilic cytoplasm
- Melanocytes + Merkel's cells are present in this layer.

E.M. - Cells are joined together by desmosomes & to b.m. by hemidesmosomes.  
- rich in ribosomes & polysomes - have intermediate filaments = Tonofilaments (prekeratin) in bundles w end in desmosomes.

#### 2. Spinous layer = Str. spinosum = Prickle cell L.

L.M. 4-8 layers of polyhedral cells e' central rounded nuclei w show mitotic figures & less basophilic cytoplasm. They have spine-like processes indicating sites of desmosomes as cells shrink during preparation

- Langerhan's cells are present in this layer.

E.M. Tonofilaments in bundles w end in desmosomes + interdigitating cell membs.

(N.B) Malpighian layer includes: basal layer + spinous layer: both show mitotic figures.

#### 3. Granular layer = Str. granulosum:

L.M. - 3-4 layers of spindle-shaped cells e' flat nuclei & basophilic granules.

E.M. - 2 types of granules:

##### (a) Coated lamellar granules:

- covered by membrane.
- contain lamellar discs = lipid bilayers. their content form lipid sheets to act as → cement (have sealing effect) & act as barrier.

##### (b) Keratohyaline granules:

large bodies not covered by membs, contain pns e' many phosphate groups so, basophilic by L.M.



#### 4. Clear Layer = Str. Lucidum:

(2)

L.M. thin, homogenous clear layer = flattened cells, Nuclei start to disappear. [Karyolysis]

E.M. - thick cell membs. joined by remnants of desmosomes.

- Nucleus & organelles disappear (lysosomal activity)
- closely packed filaments of eleidin = immature Keratin embedded in the dense matrix formed by the Keratohyaline granules.

#### 5. Horny layer = Str. Corneum:

L.M. thick acidophilic layer of scales of Keratinized dead cells.

E.M. - bags of Keratin & no nuclei or organelles

- filled & mature Keratin filaments embedded in amorphous matrix.
- their thick cell membs. are joined by remnants of desmosomes.

### [B] Non-Keratinocytes

#### 1. Melanocytes:

Origin: ectodermal. Site: just under or bet. cells of basal layer

L.M.: have rounded cell bodies & pale rounded nuclei. cannot be seen by H&E.

- have long processes w̄ extend bet. Keratinocytes. The tips of their processes end in invaginations in cells of Malpighian layer. Give Dopa +ve reaction

E.M. Have euchromatic nucleus & prominent nucleolus.

- characters of ptn. forming cells i.e. many mit., rER & well developed G.A.
- No desmosomes bet them & Keratinocytes but joined to b.m. by hemidesmosomes
- have granules called melanosomes.

#### Functions:

1. form tyrosinase enz. essential for melanin formation.

2. melanin granules lie above the nucleus to protect DNA from UVRs (by scattering them)

#### [N.B] Dopa Reaction:

Fresh section of skin is incubated & DOPA. Tyrosinase in melanocytes convert DOPA into melanin. Importance → to distinguish bet. melanocytes & melanophores  
↳ count melanocytes / area of skin.

#### Steps of melanin synthesis in melanocytes:

1. synthesis of tyrosinase starts in rER & completed in G.A.  
from w̄ vesicles bud off & called melanosomes.
2. After complete formation of melanin in " ", the granules lose tyrosinase → melanin granules w̄ migrate to the tip of the cytoplasmic processes.



## 2] Merkel's Cells:

Origin: ectodermal.

L.M. modified basal cells. Naked sensory nerve fibres end in disc like expansion under these cells → Merkel cell-neurite complex.

E.M. attached to adjacent cells by desmosomes - invaginated Nucleus.  
- cytoplasm contains → electron-dense granules like neuro-endocrine cells [APUD cells]  
↳ cytoKeratin filament (differ from those of Keratinocytes).

Functions: 1. mechanoreceptor for press.  
2. granules → paracrine regulation of epidermal cells.

## 3] Langerhans Cells: [3- 8 % of epid. cells]

Origin: stem cells in b.m → dermal bl.vs → epidermis [Mesodermal].

L.M. stellate cells bet. cells of spinous layer  
have dark N. & pale cytoplasm.  
stained by **Vital stains**.

E.M. 1-2 lysosomes + well developed G.A. + multivesicular bodies.

- **Birbeck's granules** = tennis-raquet-shaped e' Non-clear function may contain hydrolytic enzs. Irregular Nucleus

- No melanin granules, No Keratin, No desmosomes & no junctions e' Keratinocytes.

Function: 1. Act as antigen presenting cells: present antigens w contact skin to T-cells so play a role in allergic or immunological reactions.  
2. may control cell division in epidermis.

Color of skin: depend on:

1. Hb. in bl. caps. of skin (red).
2. Carotene pigment (yellow).
3. Melanin pigment (brown to black).

## Clinical Applications:

- UVRs speed tyrosinase synthesis → ↑↑ melanin formation.
- Epidermis is translucent esp. in light skinned persons, So, pale in anemia, blue in heart or lung dis. e' low O<sub>2</sub> in bl. & pink while flushing.
- Albinism: absence of melanin due to genetic defect in tyrosinase synthesis
- Psoriasis: skin disease e' ↑ proliferation of cells of Malpighian layer  
→ ↑ epidermal thickness & abnormal Keratinization. → defective skin barrier.



## II Dermis

C.T. under epidermis = 2 layers.

-4-

| Papillary layer                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Reticular layer                                                                                                                                                                                                                                                                                     |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>- thinner &amp; superficial.</li> <li>- Formed of loose c.t.</li> <li>- more cellular <math>\left\{ \begin{array}{l} \text{Fibroblasts + fat cells} \\ \text{macrophages + mast cells} \\ \text{lymphocytes.} \end{array} \right.</math></li> <li>- Fine c.t. fibres <math>\left\{ \begin{array}{l} \text{type III collagen} \\ \text{elastic fibres} \end{array} \right.</math></li> <li>- More vascular</li> <li>- Receptors : Meissner's Corpuscles</li> </ul> | <ul style="list-style-type: none"> <li>- thicker &amp; deeper.</li> <li>- dense c.t.</li> <li>- less cellular</li> <li>- collagenous bundles [type I collagen]</li> <li>- elastic fibres.</li> <li>- less vascular</li> <li>- Pacinian Corpuscles + Krause end bulb + Ruffini end Organ.</li> </ul> |

Factors Fixing epidermis to dermis :

1. basement memb. of epidermis.
2. hemidesmosomes bet. basal cells & b.m.
3. dermal papillae interdigitating w/ epidermal ridges (pegs)

Dermo-epidermal Junction :

Zigzag like interdigitations bet. dermal papillae & epidermal ridges.

F. : 1- provide attachment of epidermis to dermis.

2- ↑ surface area for nutrition of epidermis.

\* Wrinkling of skin is due to atrophy of elastic fs. of c.t. dermis.

Rapid stretch of skin → rupture of fibres in the dermis → scar tissue → white lines. In pregnancy = linea gravidarum.

Functions of skin :

1. protection : act as barrier against  $\left\{ \begin{array}{l} \text{U.V. rays (by melanin)} \\ \text{trauma, infection, dehydration (by Keratin)} \end{array} \right.$
2. sensory organs (receptors)
3. regulate body temp. (sweat + A-V. shunts)
4. excrete waste products & H<sub>2</sub>O (sweat gls).
5. synthesis of vit. D.
6. medico-legal (finger prints)
7. diagnosis of some diseases. e.g. measles, chicken pox, anaemia, jaundice, age, cirrhosis.



| Thick skin                                                                                                             | Thin skin.                                                             |
|------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------|
| Sites :- Palms & soles<br>- tips & sides of fingers & toes                                                             | - the rest of body.                                                    |
| Epidermis - thick<br>- thicker Malpighian L.<br>- thicker Granular L (2-4 Ls)<br>- Clear L present<br>- thick Horny L. | - thinner.<br>- thinner.<br>- thinner (1 L)<br>- absent.<br>- thinner. |
| dermal papilla - regular, numerous, high                                                                               | - few, irregular, small                                                |
| Appendages hair follicles<br>arrector pili ms } absent<br>sebaceous gls. }<br>More numerous sweat gls                  | - present.<br>- less numerous.                                         |

N.B. the thinnest skin in our body is in eyelid.

[Epidermal Stem Cells] ES cells.

def. :- the Follicular bulge is a region at the upper part of ext. root sheath where the arrector pili muscle is inserted. & an aggregate of undifferentiated epith. cells ES cells resides.

They do not contribute to basal stem cells of epidermis.

Function:

- Normally, ES cells → growth of hair follicles + sebaceous gls.
- If epidermis is injured or lost, ES cells migrate towards the wound surface for the initial healing of the wound.



# Skin Appendages

(6)

## A. Hairs

def: Keratinized oblique epithelial thread inserted into epidermal sheath = hair follicle.

Structure: modified part of Horny layer. Formed of:

1. Shaft: the part projecting above skin surface.
2. Root: " " embedded in the " inside the follicle.

both shaft & root are formed of:

- a. medulla = Soft Keratin.
- b. cortex = hard " contain melanin
- c. cuticle = hard "

3. Hair Follicle = downgrowth of epidermis around the " root of the hair  
formed of 3 sheaths:

\* Inner root sheath: 3 layers.

- Cuticle = scales rich in soft Keratin.
- Huxley's Layer
- Henle's " } from inside outwards.

\* Outer root sheath:

- downward continuation of epidermis
- At bottom = basal layer only.

\* C.T. sheath: c.t. dermis.

\* the outer root sheath is separated from c.t. sheath by thick basal lamina  
Glassy "memb."

## (N.B) Hair bulb

- = terminal dilatation of the hair follicle
- invaginated by vascular c.t. from dermis "hair papilla"
- contain melanocytes + matrix cells for growth of hair.

## Colour of hair:

caused by melanin pigment in the cortex produced by melanocytes in hair matrix

Grey hair: in old age melanocytes fail to produce tyrosinase.

Yellow hair: due to pheomelanin (yellow)

Baldness: hair loss due to genetic factors & sex hrs. mainly in ♂

## Arrector Pili Muscle

Smooth muscle: origin: papillary layer of dermis. insert?: c.t. sheath

It's contraction: (fear, cold = symp) → erection of hair, depression of skin (goose)  
skin



## C. Nails

def: plates of Keratinized epith. cells on dorsum of distal phalanx.

formed of: Nail plate + free edge + root (in nail groove, covered by nail fold)

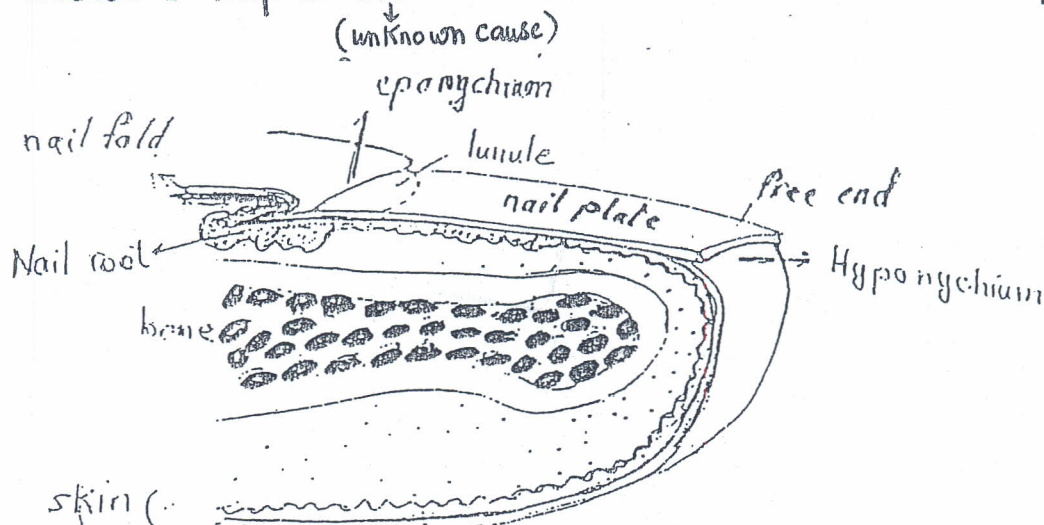
Proximal nail fold: skin fold w covers the root = **eponychium** or cuticle.

Lateral " ": 2 skin folds that cover the lat. sides of the nail.

Nail bed = area under the nail plate  $\rightarrow$  epidermal cells = thin **Malpighian L.** (sterile matrix)  
 $\downarrow$  **dermis**: highly vascular e' no papillae.

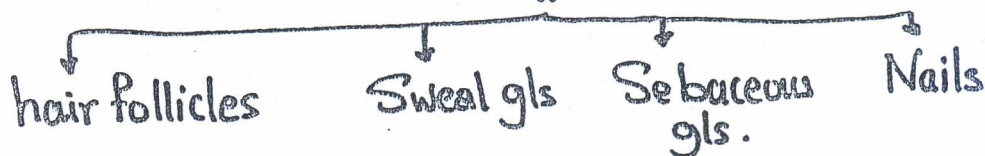
Nail Matrix: Malpighian cells lining the nail groove from w the nail grows.

Lunule: crescent-shaped white area at the base of the nail plate.



Nail

Integument = skin + Appendages





## B Glands of Skin

### a. Eccrine sweat glands      b. Apocrine sweat glands

| a. Eccrine sweat glands |                                                                                                                                                             |        | b. Apocrine sweat glands                                                                          |       | Sebaceous gl.                                                                                                                                            |
|-------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|--------|---------------------------------------------------------------------------------------------------|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| Type                    | Simple                                                                                                                                                      | coiled | tubular                                                                                           | gland |                                                                                                                                                          |
| Mode of secretion       | Merocrine (by exocytosis)                                                                                                                                   |        | Apocrine (apex lost e' secretion)                                                                 |       |                                                                                                                                                          |
| Site                    | All over the body except in glans penis & nail bed more in thick skin.                                                                                      |        | - thin skin of axilla, pubic & perineal areas.<br>- larger e' wider lumen                         |       | - associated e' hair follicles.<br>- rarely about hairs: eye lid                                                                                         |
| Acini                   | Smaller e' narrow lumen                                                                                                                                     |        |                                                                                                   |       | - 1 or 2 pear-shaped alveoli<br>- lined e'<br>- basal flat stem cells to replace<br>- central polyhedral cells e' central nuclei & vacuolated cyt. (fat) |
|                         | (1) Large pale [Clear] cells<br>- more numerous<br>- broad base & narrow apex<br>- pale cytoplasm (glycogen)<br>- intercellular canaliculi present bet them |        | (2) Small dark cells.<br>- less<br>- narrow base & broad apex.<br>- dark granular Cyt. (glycogen) |       |                                                                                                                                                          |
| Ducts                   | Spiral course in epidermis & open into                                                                                                                      |        | * hair follicle                                                                                   |       | Short, open into upper 1/3 of hair follicle                                                                                                              |
|                         | * epidermis                                                                                                                                                 |        |                                                                                                   |       |                                                                                                                                                          |
|                         | lined e' 2 layers of cubical cells in epidermis it is just spaces bet. epid. cells.                                                                         |        |                                                                                                   |       | lined e' st. sq. continuous e' the out. root sheath.                                                                                                     |
| Function                | Clear watery sweat<br>[H <sub>2</sub> O + NaCl + urea + ammonia]                                                                                            |        | - Viscid milky sweat rich in ptn.<br>Odourless<br>function at puberty                             |       | F. secrete sebum (oily)<br>- prevent cracking of skin<br>- anti bact & anti fungal<br>* disturbed secretion → acne                                       |



## B Glands of Skin

### a. Eccrine sweat glands      b. Apocrine sweat glands

| 1 Type              | Simple                                                                                                                                                  | coiled                                                                                                                          | tubular | gland |
|---------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|---------|-------|
| 2 Mode of secretion | Merocrine (by exocytosis)                                                                                                                               |                                                                                                                                 |         |       |
| 3 Site              | All over the body except in glans penis & nail bed more in thick skin.                                                                                  |                                                                                                                                 |         |       |
| 4 Acini             | Smaller e' narrow lumen                                                                                                                                 | Larger e' wider lumen                                                                                                           |         |       |
|                     | lined e' 1 layer of cuboidal cells surrounded by myoepith. cells<br>2 types                                                                             |                                                                                                                                 |         |       |
|                     | (1) Large pale [Clear] cells<br>- more numerous<br>- broad base & narrow apex<br>- pale cytoplasm (glycogen)<br>- intercellular spaces present bet them | (2) Small dark cells.<br>- less<br>- narrow base & broad apex.<br>- dark granular Cyt. (glycogen). <sup>REA</sup> <sub>3A</sub> |         |       |
| 5 Ducts             | Spiral course in epidermis & open into * hair follicle                                                                                                  |                                                                                                                                 |         |       |
|                     | * epidermis                                                                                                                                             |                                                                                                                                 |         |       |
|                     | lined e' 2 layers of cubical cells in epidermis it is just spaces bet. epid. cells.                                                                     |                                                                                                                                 |         |       |
| 6 Function          | Clear watery sweat<br>[H <sub>2</sub> O + NaCl + urea + ammonia]                                                                                        | Viscid milky sweat rich in ptn.<br>Odourless<br>bact decomposition<br>function at puberty                                       |         |       |

|                                                                                                                                             |                                                                                                |
|---------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|
| Simple or s. branched alveolary                                                                                                             | Apocrine (apex lost e' secretion) exocytosis<br>- thin skin of axilla, pubic & perineal areas. |
| Holocrine: whole cell dies & lost e' permeis thin skin secretion (Lusosa)<br>- associated e' hair follicles.<br>rarely about hairs: eye lid |                                                                                                |
| 1 or 2 pear-shaped alveoli                                                                                                                  |                                                                                                |
| lined e':                                                                                                                                   |                                                                                                |
| 1. basal flat stem cells to replace                                                                                                         |                                                                                                |
| 2. central polyhydral cells e' contain nuclei & vacuolated cyt. (fat)                                                                       |                                                                                                |
| Short, open into upper 1/3 of hair follicle                                                                                                 |                                                                                                |
| lined e' / st. sq. continuous e' the out. root sheath.                                                                                      |                                                                                                |
| F. secrete sebum (oily)                                                                                                                     |                                                                                                |
| - prevent cracking of skin                                                                                                                  |                                                                                                |
| - anti bact & anti fungal                                                                                                                   |                                                                                                |
| * disturbed secretion → acne or eczema                                                                                                      |                                                                                                |

### [2] Sebaceous gl.

|                                             |                                                                                                           |
|---------------------------------------------|-----------------------------------------------------------------------------------------------------------|
| Simple or s. branched alveolar              | Holocrine: whole cell die & lost e' secretion (associated e' hair follicles. rarely about hairs: eye lid) |
| 1 or 2 pear-shaped alveoli                  | lined e':                                                                                                 |
| 1. basal flat stem cells to top             | 2. central polyhedral cells e' contain nuclei & vacuolated cyt. (fat)                                     |
| Short, open into upper 1/3 of hair follicle | lined e' (st. sq.) continuous e' the cut. root sheath.                                                    |
| F. secrete sebum (oily)                     | - prevent cracking of skin                                                                                |
| - anti bact & anti fungal                   | * disturbed secretion → acne or pimples                                                                   |